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THE HEART IN OLD AGE. A STUDY OF 700 PATIENTS SEVENTY-FIVE YEARS OF AGE AND OLDER. By FREDRICK A. WILLIUS, M.D. 1

THE TREATMENT OF THE GASTROCARDIAC SYNDROME (GASTRIC CARDIOPATHY) By Privy Counsellor L. ROEMHELD, M.D. 13

AN ANALYSIS OF ONE HUNDRED EXAMPLES OF CARDIAC PAIN IN PRIVATE PRACTICE. By LOUIS FAUGÈRES BISHOP, M.D., Sc.D., and LOUIS FAUGÈRES BISHOP, JR., M.D. 19

RHEUMATIC FEVER IN ADULT PORTO RICAN IMMIGRANTS. By ERNST P. BOAS, M.D. 25

THE CASE FOR AND AGAINST THE OPERATIVE TREATMENT OF ANGINA PECTORIS. By WALLACE M. YATER, M.D., and ARTHUR P. TREWHELLA, M.D. . . . 35

A NEW AND SIMPLE MECHANICAL RETRACTOR FOR ABDOMINAL SURGERY. By JOHN R. O'SULLIVAN, M.D., and BERNARD A. O'CONNOR, M.D. 43

THE SPECIFIC DYNAMIC ACTION OF FOOD IN ABNORMAL STATES OF NUTRITION. By J. M. STRANG, M.D., H. B. McCLUGAGE, PH.D., with the technical assistance of M. A. BROWNLEE, R.N. 49

EXTRA-POLLEN HYPERSENSITIVITY—A MOST IMPORTANT CONSIDERATION IN THE TREATMENT OF HAY FEVER. By H. HAROLD GELFAND, M.D. 81

APPENDICITIS IN CHILDREN. By LESLIE W. TASCHE, M.D. 86

A UNIQUE ANOMALY OF THE BILIARY TRACT. COMMUNICATIONS BETWEEN CYSTIC AND HEPATIC DUCTS WITH OCCLUSION OF COMMON DUCT AND SEPARATE ENTRANCES INTO THE DUODENUM. By ANTONIO GENTILE, M.D. 95

INTRAHEPATIC LITHIASIS. By HARRY KOSTER, M.D., F.A.C.S., and I. E. GERBER, M.D. 99

OBSERVATIONS ON THE CLINICAL APPLICATION OF THE URINE SEDIMENT COUNT (ADDIS). By WILLIAM GOLDRING, M.D. 105

DISTURBANCES IN HANDWRITING AND CLUMSINESS AS SIGNS OF TOXIC GOITER. By HENRY J. VANDEN BERG, M.D., F.A.C.S. 114

THE RELATION OF BROCA'S CENTER TO LEFTHANDEDNESS. By KARL ROTHSCHILD, M.D. 116

INDEX TO PHYSICIANS' SUPPLIES . . . . . ADV. PAGE 46

Contents continued on page x

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HOBART AMORY HARE, B.Sc., M.D., LL.D.

HOBART AMORY HARE, B.Sc., M.D., LL.D.

The death of Dr. Hobart Amory Hare, early on the morning of June 15, 1931, closed a career of distinguished merit. Born in Philadelphia sixty-eight years ago, son of Bishop William Hobart Hare and Mary Amory Howe Hare, he came of a long line of ancestors eminent not alone in the church, but also in the realm of applied science, from whom he inherited a rich mental endowment.

Following a preparatory education at the Episcopal Academy of Philadelphia, he entered the University of Pennsylvania, was graduated in Medicine in 1884, received the degree of B.S. in 1885, and soon thereafter went abroad and pursued studies at Berne, Leipsic and London, chiefly concerned with physiologic research.

Shortly after his return, well equipped for the position, he was appointed Lecturer in Physiology in the Biological Department of the University of Pennsylvania and began his admirable activities along the lines of original research, especially related to the physiologic action of drugs, and speedily demonstrated his unusual ability in this field of scientific endeavor.

His aptitude for research work became evident even in his student days, in that on his graduation he was awarded the Faculty Prize for his thesis "The Influence of Quinin on the Blood." During the first six years after his graduation he was thrice the recipient of the Fiske Fund Prize of the Rhode Island Medical Society, won the Boylston Prize of Harvard ("Fever and Drugs Which Control It"), divided with Dr. Edward Martin the Cartwright Prize ("Studies in Respiration"), and the Warren Triennial Prize of the Massachusetts General Hospital ("Intestinal Obstruction"), and with Dr. Christian, of France, the prize offered by the Royal Academy of Belgium for a "Treatise on the Pathology and Treatment of Epilepsy," and had the unique honor of receiving the Fothergillian Gold Medal of the Medical Society of London for his essay on "Mediastinal Disease," being the only American who has ever obtained this distinction.

Even at this early period of his career the clinical side of medicine attracted his attention, and his attainments in this respect were recognized by the University of Pennsylvania in his appointment in 1890 as Clinical Professor of Diseases of Children.

One year later he was called by the authorities of the Jefferson Medical College of Philadelphia to fill the chair of Therapeutics and Materia Medica, later enlarged by his selection as Professor of Clinical Medicine and as Physician to the Jefferson Hospital.

For forty years he fulfilled the duties of these positions with an ability unexcelled during that period by any member of the medical staff of this distinguished Institution, as thousands of her alumni who were the happy beneficiaries of his instruction will readily attest.

As one of the editors, first of the University Medical Magazine, later, for a brief period, of The Medical News of Philadelphia, and

subsequently, for many years, of the Therapeutic Gazette, he displayed in his editorials his happy faculty of careful appraisement of clinical observations and therapeutic values. He was also editor, since its foundation in 1899, of Progressive Medicine, published by the same firm as publishes this journal, a quarterly digest which has been most useful and educationally valuable to the English-speaking medical world.

As a teacher, blessed with a facility and clarity of expression, he held his student audiences in rapt attention as he expounded the physiologic action of drugs and the various indications for their employment in the cure and amelioration of disease, and practically demonstrated their value in his rich clinical service at the Hospital.

Speedily he established his reputation as a consultant. Skillful in his physical examinations, accurate in his analyses of the symptoms-complex, wise in his therapeutic recommendations based on his unusual knowledge of the physiologic action of remedial agents, his services were in constant demand.

In spite of his crowded hours as editor, teacher, practitioner and consultant, Dr. Hare found time to write a number of sterling books and monographs, to edit systems of composite authorship and to make numerous important contributions to current medical literature, representing a product of distinguished work which is little short of amazing. Of these his "Practical Therapeutics" and his "Practical Diagnosis" achieved the greatest success, the former passing through twenty-two and the latter through nine editions in order to satisfy the universal demand.

His distinguished services in the domain of medicine were emphasized by the Trustees of the University of Pennsylvania in the bestowal of the honorary degree of LL.D. in 1900. He was President of the College of Physicians of Philadelphia, 1925–1927.

As a member of the Board of City Trusts he displayed an ability in comprehending the extensive business interests of this important Committee which commanded the lasting admiration of his colleagues. Deeply interested in Girard College and Wills Hospital, his efforts in their behalf yielded results of high importance.

During the Great War he served his country with fine fidelity as Lieutenant Commander in the Navy.

Dr. Hare's career demonstrated the inestimable value of laboratory training, research and the spirit of research in laying the foundation for a teacher of the art and science of medicine, for a sound practitioner, and for a safe and well-informed consultant. To all these tasks, faithfully performed, he lent a new vitality. He believed thoroughly in his mission: to train medical students for their careers to be devoted to the relief of human suffering and the prolongation of human life. His own life he lived abundantly; he gave richly of the best that was in him. He set his distinctive mark on our science. He will be missed as few men are.

G. E. DE SCHWEINITZ.

THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

JULY, 1931

ORIGINAL ARTICLES.

THE HEART IN OLD AGE.*

A Study of 700 Patients Seventy-five Years of Age and Older.

By Fredrick A. Willius, M.D.,

Head of Section on Cardiology, The Mayo Clinic; Associate Professor of Medicine, The Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota, Rochester, Minn.

In a period of sixty-five years fifteen years have been added to the span of life. This prolongation of life has been largely affected by decrease in mortality in infancy and childhood. However, there is no evidence at hand to indicate an increased expectation of life for adults or the aged.

A study of present-day charts of death rate reveals the fact that the improvement made in the reduction of the death rate from tuberculosis and pneumonia, for instance, is being counterbalanced by the increasing death rate from heart disease. Dublin clearly emphasized this observation.

In a consideration of the possibility of extending human life, Dublin, in 1922, constructed a hypothetic life table based on the life table for states which were in the registration area of the United States in 1910. He expressed the most favorable mortality rate that might be anticipated in view of knowledge and actual accomplishments at the time he was writing. According to his figures, the expectation of life at birth was approximately sixty-five years.

* Submitted for publication January 16, 1931.

Therefore, if sixty-five years may be said to represent the optimal expectation of present-day life, and if heart disease is the leading cause of death today, it seems desirable to investigate the status of the heart in aged persons.

The Present Study. *Material.* In order to obtain cases in which special consideration was given to the cardiovascular system, the records of all patients who had undergone electrocardiographic examination at The Mayo Clinic, from August 1, 1914, to January 1, 1930, were considered, and from these, cases of aged persons were selected. In order to avoid approximating the average accepted expectation of life, sixty-five years, the low age limit for patients in this study was arbitrarily set at seventy-five years. The oldest patient was ninety-six years of age. Under these limitations 700 cases were available for study, representing an incidence of 1.1 per cent of persons who had undergone electrocardiographic examination.

It must be acknowledged that the results of critical analysis of this selected material are not entirely comparable to those that might be derived from a similar number of cases of patients of the same ages as those selected taken from the general population or from other limited fields of the general population. It must be assumed that the majority of aged patients who seek medical advice at a clinic which is more or less distant from their homes have ailments that may not exist to the same degree and extent among patients in other groups.

Age. Owing to the fact that this study represents patients in seventeen separate years of life, it seemed desirable to simplify the statistics by considering the ages in combined periods of two years.

Nearly half (47 per cent) of the cases occurred in the age group seventy-five and seventy-six years. (Table I.) A progressive diminution in incidence occurred as age increased, as would be anticipated. Only 4 cases (0.5 per cent) occurred in the oldest age group which was enlarged to include patients, ninety-one to ninety-six years of age. Six hundred four (86.3 per cent) of the cases occurred among patients who had not reached the eighty-first year of life.

TABLE I.—AGE INCIDENCE.

Age group, years.	Cases.	Per cent.
75 and 76	329	47.0
77 and 78	185	26.4
79 and 80	90	12.9
81 and 82	46	6.6
83 and 84	23	3.3
85 and 86	14	2.0
87 and 88	9	1.3
91 to 96	4	0.5
Total	700	100.0

Sex Incidence. The incidence of males to females in this series was almost 5 to 1. There were 571 males (81.5 per cent) and 129

females (18.5 per cent). The consistent predominance of males in all age groups is evident in Table II.

TABLE II.—SEX INCIDENCE.

Age group, years	Cases.	Males.		Females.	
		Number.	Per cent.	Number.	Per cent.
75 and 76	329	259	78.7	70	21.3
77 and 78	185	152	82.1	33	17.9
79 and 80	90	76	85.5	14	14.5
81 and 82	46	37	80.4	9	19.6
83 and 84	23	22	95.6	1	4.4
85 and 86	14	13	92.8	1	7.2
87 and 88	9	8	88.8	1	11.2
91 to 96	4	4	100.0		
Total	700	571	81.5	129	18.5

The marked disproportion in sex incidence in the series of 700, including those who had heart disease and those who had not, was due in large measure to the fact that 186 patients (26.5 per cent) came to the Clinic because of the disease which so often affects aged men, benign prostatic hypertrophy. Also, the well-recognized greater incidence of heart disease among males influenced the sex incidence to a considerable degree, in this series; the ratio of men to women who had heart disease was 5 to 1. This difference in incidence is probably somewhat greater than that which would occur in a random selection of patients of similar age groups.

Blood Pressure. The blood pressure of all patients in this series was investigated. In many cases the average of several readings was taken; in others the records represent only a single reading. Owing to the fact that some of the later age groups were small, the statistical error obviously was greater than that which would occur with larger groups of cases. The figures, however, give the general tendency of blood pressure in the aged, especially with reference to hypertension. Studies of blood pressure that would allow comparison between the sexes was not attempted owing to the relatively small number of women.

Alvarez and Stanley, in studying the blood pressure of 6000 prisoners, ranging in age from fifteen to eighty-four years, found that the modal or most typical pressure varied little from youth to old age. Their observations also indicated that the mean or arithmetic average pressure did not increase until after the fortieth year. Among the male prisoners the percentage with systolic pressures of more than 140 mm. of mercury, in the age group twenty to forty years, remained constant, suggesting that those persons who had hypertensive readings at the age of forty years had similar readings at the age of twenty years. A pressure of 115 mm. is just as normal, these authors stated, and a pressure of 140 mm. is just as abnormal, in an old man as in a young one. They also found that diastolic pressure tends to rise several years in advance of systolic pressure.

In studying the systolic blood pressures in young men, Diehl and Sutherland based their investigation on 5122 students who entered the University of Minnesota. They found systolic pressures of 140 mm. or more in 16.2 per cent of their group examined in 1922 and in 9 per cent of their groups examined in 1923 and in 1924. In the latter groups systolic readings of 160 mm. or more occurred in 0.5 per cent and of 170 mm. or more in 0.1 per cent. Believing that excitement and nervous influences might account for the discrepancy between the group examined in 1922 and those examined respectively in 1923 and 1924, 209 students of the 389 with systolic readings of 140 mm. or more were reëxamined, and only 15 per cent of these proved to have persistent hypertension.

In the present group 521 aged patients (74.5 per cent) had systolic blood pressures of 140 mm. or more. (Table III.) This is opposed to the results in young and middle-aged persons. Of patients with systolic blood pressure of 140 mm. or more 492 (70.3 per cent) were in the first three age groups, that is, from the age of seventy-five to eighty years, inclusive. Only 68 patients (9.7 per cent) had systolic blood pressures of 200 mm. or more, and these, likewise, were chiefly in the first three age groups. The systolic blood pressures of 414 patients (59.1 per cent) were within the range of 130 to 180 mm.

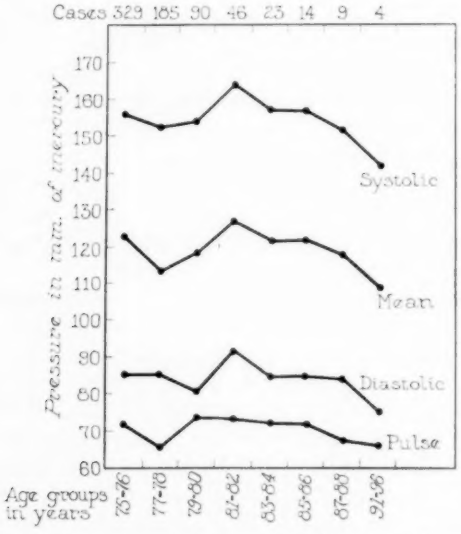

FIG. 1.—Average blood pressure and pulse readings.

The average systolic pressure according to age groups is shown in Fig. 1. These averages are not without considerable error owing to the great variation of the individual components of the various age groups. The average systolic reading in all age groups was

more than 140 mm.; the lowest average for any age group was 142.5 mm. The peak occurred in the age group eighty-one and eighty-two years in which the average systolic pressure was 164.2 mm.

The mean pressure or arithmetic average of the systolic and diastolic pressures (Tables III, IV and V) varied in a fairly parallel manner with the systolic pressure. (Fig. 1.) In a study of this type the mean pressure has little significance, owing to the fact that it is profoundly influenced by either abnormally high or abnormally low readings. The range of average mean pressures was 109 to 127.8 mm.

The diastolic blood pressure taken by itself did not parallel the systolic. Only 282 patients (40.3 per cent) had diastolic pressures of 90 mm. or more, which means that approximately one-third of the patients with systolic pressure greater than 140 mm. had normal or practically normal diastolic pressures. Only 75 patients (10.7 per cent) had diastolic pressures of 110 mm. or more. The diastolic blood pressure was between 60 and 120 mm. in the majority of cases; that is, in 464 (66.3 per cent). The averages of diastolic blood pressure, according to age groups, are shown in Fig. 1. With the exception of one age group, eighty-one and eighty-two years, the average diastolic pressures were less than 90 mm.

Pulse pressure was 60 mm. or more in 487 cases (69.6 per cent). (Table V.) Pulse pressures of 90 mm. or more occurred in 145 cases (20.7 per cent). The general trend of pulse pressure was in the range of 50 to 100 mm. where 504 cases (72 per cent) were placed. The averages of pulse pressure are shown in Fig. 1; all were in excess of 60 mm.; the highest average was 73 mm. and was recorded in the age group eighty-one and eighty-two years.

It is evident from the studies of blood pressure of the persons who comprised this aged group that hypertension is the rule; systolic blood pressures of 140 mm. or more occurred in 74.5 per cent, and diastolic blood pressures of 90 mm. or more occurred in 40.3 per cent of the cases.

Distinctly low blood pressure occurred infrequently; systolic blood pressure was less than 120 mm. in only 9.3 per cent and diastolic blood pressure less than 70 mm. in only 11 per cent of the cases.

Patients Without Clinical Evidence of Heart Disease. In a consideration of aged patients the failure to elicit symptoms and signs of heart disease does not by any means indicate that the heart is normal. The extremely high incidence of arteriosclerotic cardiovascular changes in senescence renders the possibility of finding a perfectly normal heart very remote. Robertson has stated that a normal heart is practically never observed at necropsy in a person who has passed the age of seventy-five years. Therefore, the group of patients under immediate consideration may be said merely not to have presented clinical evidence of heart disease. There were 315 patients (45 per cent) in this category. (Table VI.)

TABLE III.—SYSTOLIC BLOOD PRESSURE OF 700 PATIENTS SEVENTY-FIVE YEARS OF AGE AND OLDER.

Blood pressure, mm. of mercury.	Age group, years.														Total.	
	75 and 76.		77 and 78.		79 and 80.		81 and 82.		83 and 84.		85 and 86.		87 and 88.		91 to 96.			
	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
90 to 99	4	80.0	1	20.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	5	0.7
100 to 109	14	66.6	3	14.3	4	19.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	21	3.0
110 to 119	20	51.3	7	17.9	5	12.8	3	7.7	2	5.1	1	2.6	1	2.6	0	0.0	39	5.6
120 to 129	24	40.0	18	30.0	11	18.3	6	10.0	0	0.0	1	1.7	0	0.0	0	0.0	60	8.6
130 to 139	28	51.8	13	24.1	6	11.1	3	5.5	0	0.0	1	1.9	2	3.7	1	1.9	54	7.7
140 to 149	48	46.2	25	24.0	16	15.4	4	3.8	6	5.8	3	2.9	0	0.0	2	1.9	104	14.9
150 to 159	35	41.2	26	30.6	11	12.9	6	7.1	1	1.2	2	2.3	3	3.5	1	1.2	85	12.1
160 to 169	38	37.4	37	36.4	13	12.7	2	1.9	8	7.8	2	1.9	2	1.9	0	0.0	102	14.6
170 to 179	43	62.3	14	20.3	6	8.7	5	7.3	0	0.0	1	1.4	0	0.0	0	0.0	69	9.9
180 to 189	23	39.7	20	34.5	3	5.2	6	10.3	6	10.3	0	0.0	0	0.0	0	0.0	58	8.3
190 to 199	16	45.7	8	22.9	6	17.1	4	11.4	0	0.0	1	2.9	0	0.0	0	0.0	35	5.0
200 to 209	15	71.4	4	19.0	1	4.8	0	0.0	0	0.0	0	0.0	1	4.8	0	0.0	21	3.0
210 to 219	5	33.3	2	13.3	3	20.0	4	26.7	0	0.0	1	6.7	0	0.0	0	0.0	15	2.1
220 to 229	9	53.0	3	17.6	3	17.6	1	5.9	0	0.0	1	5.9	0	0.0	0	0.0	17	2.4
230 to 239	4	100.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	4	0.6
240 to 249	3	42.9	2	28.5	1	14.3	1	14.3	0	0.0	0	0.0	0	0.0	0	0.0	7	1.0
250 to 259	0	0.0	2	66.7	1	33.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	3	0.4
260 to 269	0	0.0	0	0.0	0	0.0	1	100.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
Total	329	....	185	....	90	....	46	....	23	....	14	....	9	....	4	....	700	100.0
Mean blood pressure	122.8	....	114.0	....	119.0	....	127.8	....	121.7	....	121.7	....	118.0	....	109.0			
Percentage over 140 mm.*	72.7	....	77.3	....	71.2	....	74.0	....	91.3	....	78.6	....	66.7	....	75.0			

* Total number of patients with systolic pressure of 140 mm. and over, 521 (74.5 per cent).

* Total number of patients with systolic pressure of 140 mm. and over, 521 (74.5 per cent).

TABLE IV.—DIASTOLIC BLOOD PRESSURE OF 700 PATIENTS SEVENTY-FIVE YEARS OF AGE AND OLDER.

Blood pressure, mm. of mercury.	Age group, years														Total	
	75 and 76.		77 and 78.		79 and 80.		81 and 82.		83 and 84.		85 and 86.		87 and 88.		91 to 96.			
	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
40 to 49	3	100.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	3	0.4
50 to 59	10	62.5	1	6.3	3	18.6	0	0.0	1	6.3	0	0.0	0	0.0	1	6.3	16	2.3
60 to 69	23	39.6	16	27.6	11	19.0	4	6.9	2	3.5	1	1.7	1	1.7	0	0.0	58	8.3
70 to 79	67	50.4	38	28.6	16	12.0	9	6.8	1	0.7	0	0.0	2	1.5	0	0.0	133	19.0
80 to 89	82	39.4	64	30.8	26	12.5	12	5.8	10	4.8	7	3.4	4	1.9	3	1.4	208	29.7
90 to 99	65	52.0	33	26.4	17	13.6	3	2.4	3	2.4	3	2.4	1	0.8	0	0.0	125	17.9
100 to 109	38	46.3	17	20.7	12	14.6	7	8.5	5	6.2	3	3.7	0	0.0	0	0.0	82	11.7
110 to 119	26	61.9	6	14.3	3	7.1	6	14.3	0	0.0	0	0.0	1	2.4	0	0.0	42	6.0
120 to 129	6	40.0	5	33.3	1	6.7	2	13.3	1	6.7	0	0.0	0	0.0	0	0.0	15	2.2
130 to 139	5	55.5	1	11.1	1	11.1	2	22.3	0	0.0	0	0.0	0	0.0	0	0.0	9	1.3
140 to 149	3	37.5	4	50.0	0	0.0	1	12.5	0	0.0	0	0.0	0	0.0	0	0.0	8	1.1
150 to 159	1	100.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
Total	329	....	185	...	90	...	46	...	23	...	14	...	9	...	4	...	700	100.0
Mean blood pressure	122.8	....	114.0	...	119.0	...	127.8	...	121.7	...	121.7	...	118.0	...	109.0			
Percentage over 90 mm.*	43.8	....	35.7	...	37.8	...	45.7	...	39.2	...	42.9	...	22.3	...	0.0			

* Total number of patients with diastolic pressure of 90 mm. and over, 282 (40.3 per cent).

TABLE V.—PULSE PRESSURE OF 700 PATIENTS SEVENTY-FIVE YEARS OF AGE AND OLDER.

Pressure, mm. of mercury.	Age group, years.																Total.	
	75 and 76.		77 and 78.		79 and 80.		81 and 82.		83 and 84.		85 and 86.		87 and 88.		91 to 96.			
	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number	Per cent.
20 to 29	8	80.0	1	10.0	0	0.0	0	0.0	1	10.0	0	0.0	0	0.0	0	0.0	10	1.4
30 to 39	17	63.0	6	22.2	2	7.4	1	3.7	0	0.0	0	0.0	1	3.7	0	0.0	27	3.9
40 to 49	34	44.7	18	23.8	14	18.4	7	9.2	0	0.0	2	2.6	1	1.3	0	0.0	76	10.9
50 to 59	52	52.0	14	14.0	17	17.0	9	9.0	4	4.0	2	2.0	1	1.0	1	1.0	100	14.3
60 to 69	47	35.6	47	35.6	16	12.1	8	6.1	7	5.3	4	3.1	2	1.5	1	0.7	132	18.8
70 to 79	65	51.6	38	30.2	15	11.9	4	3.2	0	0.0	2	1.5	1	0.8	1	0.8	126	18.0
80 to 89	39	46.4	24	28.6	8	9.5	3	3.6	7	8.3	0	0.0	2	2.4	1	1.2	84	12.0
90 to 99	32	51.6	18	29.0	2	3.2	4	6.5	3	4.8	2	3.2	1	1.7	0	0.0	62	8.9
100 to 109	12	35.3	1	32.4	6	17.6	4	11.8	1	2.9	0	0.0	0	0.0	0	0.0	34	4.9
110 to 119	15	57.7	4	15.4	3	11.5	4	15.4	0	0.0	0	0.0	0	0.0	0	0.0	26	3.7
120 to 129	3	25.0	1	8.3	5	41.7	2	16.7	0	0.0	1	8.3	0	0.0	0	0.0	12	1.7
130 to 139	1	25.0	1	25.0	1	25.0	0	0.0	0	0.0	1	25.0	0	0.0	0	0.0	4	0.6
140 to 149	2	40.0	2	40.0	1	20.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	5	0.7
150 to 159	1	100.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
160 to 169	1	100.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
Total	329	....	185	....	90	....	46	....	23	....	14	....	9	....	4	....	700	100.0
Mean blood pressure	122.8	....	114.0	....	119.0	....	127.8	....	121.7	....	121.7	....	118.0	....	109.0			
Percentage over 90 mm.*	66.3	....	79.0	....	63.4	....	63.1	....	78.3	....	71.5	....	66.7	....	25.0			

* Total number of patients with pulse pressure of 60 mm. and over, 487 (69.6 per cent).

TABLE VI.—INCIDENCE OF HEART DISEASE IN VARIOUS AGE GROUPS AND IN ENTIRE GROUP.

Age group, years.	Cases.	Patients with evidence of heart disease.		Patients without evidence of heart disease.	
		Number.	Per cent.	Number.	Per cent.
75 and 76	329	160	48.6	169	51.4
77 and 78	185	89	48.1	96	51.9
79 and 80	90	53	58.8	37	41.2
81 and 82	46	38	82.6	8	17.4
83 and 84	23	21	91.3	2	8.7
85 and 86	14	13	92.8	1	7.2
87 and 88	9	8	88.8	1	11.2
91 to 96	4	3	75.0	1	25.0
Total	700	385	55.0	315	45.0

The sex incidence was the same as that in the entire series, namely, males, 262 (79.8 per cent), and females, 53 (20.2 per cent), or a ratio of 5 to 1.

In Table VII is found the diversified list of diagnoses made in this group of cases, and from this it is apparent that very few relatively normal old people were available for study.

TABLE VII.—CLINICAL DIAGNOSES IN CASES WITHOUT CLINICAL EVIDENCE OF HEART DISEASE.

Diagnosis.	Cases.	Diagnosis.	Cases.
Benign prostatic hypertrophy	136	Glaucoma	2
Carcinoma	48	Calculi in urinary bladder	2
Arteriosclerosis	25	Uterine prolapse	2
Chronic arthritis	15	Chronic nephritis	2
Peptic ulcer	10	Pulmonary emphysema	2
Chronic cholecystitis	10	Exophthalmic goiter	2
Negative examinations	8	Constipation	2
Adenomatous goiter with hyperthyroidism	7	Thrombophlebitis of leg	1
Diabetes mellitus	7	Asthmatic bronchitis	1
Hernia	7	Esophageal diverticulum	1
Pernicious anemia	6	Syphilis	1
Cataract	4	Ulcer of urinary bladder	1
Urethral stricture	4	Neuritis	1
Trifacial neuralgia	3	Angioma	1
Parkinson's disease	2	Diverticulum of urinary bladder	1
		Lymphatic leukemia	1

The electrocardiograms in this group did not reveal significant abnormalities. Premature contractions were found at the time of examination in 108 cases (34.3 per cent). They were of ventricular origin in 57 cases, of auricular origin in 32 cases and of nodal origin in 19 cases.

Patients With Clinical Evidence of Heart Disease. This group comprised 385 patients (Table VI), or 55 per cent of the entire series. The sex incidence was essentially the same as that in the entire group: males, 309 (80.3 per cent), and females, 76 (19.7 per cent), a ratio of 5 to 1.

The types of heart disease found in a group of aged patients are

very limited. Hypertensive or coronary disease comprised 381 (98.9 per cent) cases in the group studied.

In making clinical differentiation between cases of hypertensive heart disease and cases of coronary sclerosis I am mindful of the fact that these diseases coëxist very commonly and, therefore, that the arbitrary division as given here is not without error. However, it was impossible accurately to select a group in which the two conditions were continued; therefore, the cases were classified according to the dominant clinical evidence, either as instances of hypertensive heart disease or of coronary disease. Further to emphasize the coëxistence of these diseases, the records of necropsy at The Mayo Clinic disclose such coëxistence in approximately 80 per cent of the cases in which either disease occurs.

Predominant hypertensive heart disease occurred in 209 cases, or 54.2 per cent. (Table VIII.)

TABLE VIII.—TYPES AND INCIDENCE OF HEART DISEASE.

Type of cardiac disease.	Age group, years.								Total.	
	75 and 76.	77 and 78.	79 and 80.	81 and 82.	83 and 84.	85 and 86.	87 and 88.	91 to 96.	No.	Per cent.
Hypertensive heart disease	92	44	28	23	12	7	3	0	209	54 2
Coronary sclerosis with angina pectoris	24	12	3	3	4	0	0	1	47	12 2
Coronary sclerosis without angina pectoris	44	31	20	12	4	6	5	2	124	32 2
Coronary thrombosis	0	0	1	0	0	0	0	0	1	0 3
Syphilitic aortitis	0	1	1	0	1	0	0	0	3	0 8
Chronic endocarditis with aortic insufficiency	0	1	0	0	0	0	0	0	1	0 3

Coronary disease occurred in 172 cases (44.7 per cent) and was represented by 47 cases with the anginal syndrome, 124 cases without painful seizures and only 1 case with coronary thrombosis. The extremely small incidence of coronary thrombosis (0.3 per cent) in this series of aged patients substantiates previous observations that its occurrence is most common between the fiftieth and the seventieth years of life. This may indicate that the majority of persons who attain advanced age are permitted to do so, in part at least, because they possess a sturdy and adequate coronary arterial tree, an endowment that is denied many other persons. This concept finds further support in the fact that, although the incidence of coronary sclerosis in this group was relatively high, acute occlusion was exceptional. This suggests that even in the presence of coronary disease cardiac nutrition is sufficient to permit life to be protracted definitely in excess of the accepted average.

The rarity of other forms of heart disease is evident; only 4 cases

(1.1 per cent) were recorded. There were 3 cases of syphilitic aortitis and 1 case of nonsyphilitic aortic insufficiency. It is not unlikely, of course, that in the analysis of a larger group of aged patients other forms of heart disease occasionally would be encountered.

Congestive heart failure at the time of examination occurred in 85 cases (22.1 per cent). More than half (54.1 per cent) of the patients who displayed this syndrome had dominant hypertensive heart disease.

The significant electrocardiographic abnormalities which occurred in cases of evident heart disease are shown in Table IX. *T* wave negativity occurred with greatest frequency; it was recorded in 96 cases (24.9 per cent). This abnormality occurred predominantly in Lead I; the incidence was 57 cases (14.8 per cent). It is interesting to observe that no instance of *T* wave negativity occurred after the eighty-fourth year; in other words, none in the oldest 27 patients of the entire group.

TABLE IX.—ELECTROCARDIOGRAPHIC CHANGES IN CASES OF EVIDENT HEART DISEASE.

Electrocardiographic changes	Age group, years.								Total.		
	75 and 76.	77 and 78.	79 and 80.	81 and 82.	83 and 84.	85 and 86.	87 and 88.	91 to 96.	No.	Per cent.	Group, per cent.
T wave negativity in Lead I	31	12	7	5	2	0	0	0	57	14 8	
T wave negativity in Leads I and II	6	3	2	2	0	0	0	0	13	3 4	
T wave negativity in Leads II and III	11	3	1	3	1	0	0	0	19	4 9	
T wave negativity in Leads I, II and III	2	2	1	1	1	0	0	0	7	1 8	24 9
Complete block	1	1	1	1	0	0	0	0	4	1 0	
Delayed auriculoventricular conduction	5	3	1	1	1	2	1	0	14	3 6	
Incomplete bundle-branch block	9	4	3	2	0	0	2	1	16	4 2	
Complete bundle-branch block	2	1	0	1	2	0	0	0	6	1 6	
Sino-auricular block	1	0	0	0	0	0	0	0	1	0 3	10 7
Auricular fibrillation	28	21	6	5	4	2	1	1	68	17 9	
Auricular flutter	3	0	1	0	0	0	0	0	4	1 0	18 9

Disturbances in cardiac conduction were present in 41 cases (10.7 per cent). Incomplete bundle-branch block and delayed auriculoventricular conduction were most common and occurred in 16 cases (4.2 per cent) and 14 cases (3.6 per cent) respectively. The patients who exhibited delayed auriculoventricular conduction were all subjected to the atropin test, and the prolongation in transmission of impulse remained uninfluenced.

Among electrocardiographic abnormalities auricular fibrillation

occurred with greatest frequency. It was present in 68 cases (17.9 per cent). Auricular flutter was found in only 4 cases (1 per cent).

Premature contraction occurred in 123 cases (31.9 per cent), an incidence slightly more than that in the group of patients without clinical evidence of heart disease. They were of ventricular origin in 83 cases, of auricular origin in 19 cases and of nodal origin in 21 cases.

Comment. From this study of aged patients, one gleans the impression that the majority of persons, even in the presence of evident heart disease, possess hearts of unusual quality. This impression becomes strengthened by the fact that only 85 patients (12.1 per cent of the complete series) had congestive heart failure. The heart, impaired or unimpaired by disease, that permits continuation of life to and beyond the seventy-fifth year is an organ of unusual quality.

Summary. This study is based on 700 patients seventy-five years of age and older who were carefully investigated with special reference to the cardiovascular system. The ages of the patients ranged from seventy-five to ninety-six years. Forty-seven per cent of the patients were aged seventy-five and seventy-six years. The numbers in the various age groups diminished progressively with advance in age; only 0.5 per cent were between the ages of ninety-one and ninety-six years. The ratio of the sexes was 5 men to 1 woman. Seventy and three-tenths per cent of the patients had systolic blood pressures of 140 mm. of mercury or more. Only 9.7 per cent had systolic blood pressures of 200 mm. or more. The mean blood pressure ranged from 109 to 127.8 mm. The diastolic blood pressure in 40.3 per cent of cases was 90 mm. or more. Diastolic pressures of 110 mm. or more occurred in 107 cases. Pulse pressures of 60 mm. or more occurred in 69.6 per cent of cases and readings of 90 mm. or more in 20.7 per cent. It is evident from this study that hypertension is the rule in aged patients. There were 315 patients (45 per cent) without clinical evidence of heart disease as opposed to 385 patients (55 per cent) with clinical evidence of heart disease.

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THE TREATMENT OF THE GASTROCARDIAC SYNDROME (GASTRIC CARDIOPATHY).

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The "gastrocardiac syndrome" is an expression which I coined, in 1912, in order to characterize certain hitherto little-known relations between stomach and heart, or, more generally speaking, between the digestive and circulatory systems. On the basis of extensive Roentgen ray studies I was able to demonstrate that many a so-called cardiac neurosis was, in reality, caused by some disturbance within the digestive tract. In fact, I am inclined to look upon the cardiovascular system as a sort of barometer which often registers organic or functional upheavals within the abdominal cavity and more particularly its upper left quadrant.

The "gastrocardiac syndrome," therefore, describes those disturbances of the circulatory system, and in particular the heart, which are produced by faulty function of the digestive tract, especially the stomach. Such disturbances may occur in patients both with normal or diseased hearts, and are due to one of two causes: (1) Mechanical: From dislocation of the heart and large vessels due to elevation of the left half of the diaphragm as a result of subdiaphragmatic accumulation of air, such as may be caused by various organic or functional anomalies. (2) Reflex: Through the effect of chemical and toxic substances within the stomach and intestines.

Of these two causes, the former is by far the more frequent. Whether the accumulation of air is within the stomach, the splenic flexure or generally distributed in the intestines, the diaphragm is almost always pushed upward more on the left side, because the weight of the liver restrains rightsided elevation. The heart, its free movements thus encroached upon, reacts, after a while, with disturbances of rhythm and causes definitely unpleasant sensations.

The reflex affection of the heart, which is often associated with the mechanical, is caused by a variety of ailments of the gastrointestinal tract. Among these, subacid or anacid conditions play a prominent rôle. Further, fermentation dyspepsia with marked flatulency, colitis localized in the transverse and descending colon, cholelithiasis, etc., are to be mentioned. On the other hand, ulcer or cancer of the stomach but rarely lead to cardiac disturbances.

It must, however, be admitted that not in every case does the heart become disturbed by leftsided elevation of the diaphragm. By distending the stomach with carbonic acid for experimental

studies, I found that certain individuals suffered no discomfort whatever, while others complained considerably of distress in the region of the heart. Yet, in both categories the heart itself was organically sound.

We may conclude from these experiments that the gastrocardiac syndrome can develop only if the heart responds too readily to stimuli. This may be the chief reason why we find such gastrocardiac symptoms primarily in people of middle or later life, and more particularly in patients of the wealthier classes who take but little exercise, eat too hastily and, in general, lead a life of high tension. In men dyspeptic heart symptoms occur most often in that time of life when the costal cartilages ossify and the thorax becomes rigid. Inasmuch as males are unaccustomed to costal breathing, interference with abdominal breathing such as would ensue from distention of the stomach or elevation of the diaphragm from any other cause is particularly unpleasant. Lack of habit and rigidity of the thorax render the costal type of breathing more difficult in males.

Patients with the gastrocardiac syndrome, as a rule, do not give the impression of being seriously ill. Yet they never feel quite well; they complain very frequently of distress in the left side which, usually, is diagnosed either as "nervous" or being due to some obscure heart lesion.

It is, of course, quite possible that occasionally such a patient may have a true heart disease, and in such a case the disordered stomach with its varying degrees of distention, the elevation of the diaphragm and the mechanical dislocation of the heart represent serious complications. In the majority of instances, however, one searches in vain for objective findings of cardiac affection in these patients.

Let us, then, first consider the gastrocardiac syndrome in a patient with a normal heart. The classical symptoms which, of course, need not be present in all cases with equal intensity are as follows: There is, particularly after meals, a dull and painful pressure at the left costal margin. This may take the form of anginoid distress, with pain radiating into the left arm. Pain behind the sternum is less often noticeable. Gas-producing foods, in particular carbohydrates and cellulose, seem to bring on these attacks rather readily, so that one may speak of certain idiosyncrasies. Then there is shortness of breath, an apparent inability of taking a deep breath. The abnormal distention of the stomach with air, which is often quite impressive on inspection, leads to irritation of the vagus nerve, and this again to bradycardia and extrasystole. Of this, the patient is acutely conscious, particularly if he is nervous or hears the action of his heart when lying on the left side. Or else, the irritation may give rise to tachycardia, to

vertigo and sensations of fainting, either because the cardia is kinked or the large vessels in the thorax are pressed upon; to a sense of fear or even of impending death, to syncope-like appearance, nausea, vomiting, hiccough, continued belching, etc.—in short, a complex of symptoms which at times may resemble Stokes-Adams syndrome and may assume alarming proportions, yet disappears as soon as the subdiaphragmatic air bubble has been removed by lavage of the stomach, an emetic or a purgative.

Objectively, the heart findings, as a rule, are normal if the patient has not eaten. At the height of digestion, however, the impulse of the apex is dislodged upward and outward. Percussion frequently yields loud tympanitic sound even above the left nipple, whereas there is dullness over the sternum and a relative dullness below the left clavicle. This latter phenomenon is due to the dislocation of the heart and a relative atelectasis of the upper left lung. The heart seems to lie transversely. On Roentgen ray examination it can clearly be seen how the excessive accumulation of air beneath the left diaphragm raises the apex of the heart and displaces the aorta in such a way that its ascending portion is curved toward the right side, a picture which closely resembles that of a sclerosis of the aorta. At times, however, with milder symptoms, the objective evidences of displacement are very difficult to detect.

Respiration is apt to be shallow and of the costal type. The patients complain of a multitude of dyspeptic symptoms and are discouraged because all previous medical attention has been unsuccessful. The conviction grows in them that the heart is at fault; for this reason they shun exercise, and this again leads to retention of even more gastrointestinal gas and to considerable increase in body weight, particularly if the patients, as is so often the case, are overeaters. Gradually the elevation of the diaphragm becomes more and more pronounced, and, as a direct consequence, the encroachment on the heart, the dyspnea, extrasystolia, pseudo-angina and other disagreeable sensations within the thoracic cavity are intensified. Since they know from experience that belching gives at least temporary relief, such patients try their best to eructate, and in doing so become in time more or less unconsciously air swallowers. Thus a vicious circle is established which can be broken only if the attending physician is familiar with the true state of affairs.

The basis of successful therapy must needs be the discovery of the specific cause of the subphrenic air bubble and the removal of the accumulated gas. This latter procedure will, at the same time, do away with reflex and toxic sources of dyspeptic cardiac disturbances.

We know three causes of excessive accumulation of "gas" in the stomach or intestines, namely: (1) Aërophagy, that is, the invol-

untary swallowing of air, such as we find it in certain neurasthenics, in fast eaters, in overworked and worn-out people and as a voluntary habit in patients who have found relief from belching. (2) Insufficient absorption of gastric or intestinal gas and delay in their expulsion. This is due either to increased tonus of the vagus or to anatomic changes, such as pyloric stenosis, adhesions, kinks. (3) Increased formation of gas in the gastrointestinal canal, caused by abnormal fermentation and decomposition of unsuitable food in a gastrointestinal tract whose chemism is disturbed. Not infrequently several of these specific causes of air bubbles may be in combination.

Treatment must be applied: (1) To the psychic and general condition of the patient. (2) To the digestive apparatus (dietetic and medicinal therapy). (3) To the diaphragm (physiotherapy).

As has been mentioned before, two mistakes are very commonly made by physicians. These patients are either told that they are "merely nervous" and should pay no attention to their distress in the heart region; or their condition is diagnosed as a beginning arteriosclerosis and a carbohydrate diet supported by iodin and digitalis is prescribed. Obviously, both these modes of management are equally faulty and can only lead to an even firmer conviction of a serious heart trouble. It is, therefore, doubly important to quiet the patient's fears from the very beginning, to assure him that his heart is perfectly normal and that it is only his dyspepsia which needs attention. Since digestive disturbances are so much less alarming to the laity, his mind will be set at rest. In addition, his general condition must be improved. The obese—and these form the majority—must be reduced in weight and their musculature, including that of heart and diaphragm, be strengthened.

As to dietetic treatment, all gas-forming foods which contain much cellulose, cabbage, seed vegetables or legumes, fresh bread, particularly rye bread, raw fruit in large quantities must be excluded. Buttermilk and the like is preferable to sweet milk in anacidity of the stomach. Carbonated waters are not to be advised. In general, the diet should be adapted to the personal experience of the patient and known idiosyncrasies should be taken into consideration. Overeating should at all times be avoided. Meals should be eaten slowly and the psychic side of the "pleasures of the table" emphasized. An occasional change from a vegetable-carbohydrate to a meat-fat diet sometimes yields astonishing results. In colitis the diet should be free from cellulose as far as possible, and combined with oil enemas. The meals should be small and well masticated. A mild form of exercise, such as a game of billiards or a short walk, is better than rest after eating, and abdominal massage, too, is of importance.

In the medicinal treatment of subacidity or anacidity I have seen

excellent results from pepsin combined with hydrochloric acid in large doses; where the latter is not well borne citric acid is substituted. Hyperacidity requires atropin or any of the numerous antacids on the market. Belching may be promoted by the various derivatives of valerian (validol, bornyval, etc.). Not infrequently, a gastric lavage produces a magic effect, particularly in tachycardia and especially where the air bubble is caused by a chronic gastritis.

But nothing that is done with psychotherapy, diet or medicines is complete or promises to have a lasting effect unless it is supported by physiotherapeutic measures. The purpose of these is to accelerate venous circulation in the abdominal cavity and thereby reduce accumulation of gas, particularly beneath the left diaphragm. We, therefore, should resort to abdominal massage, gymnastics, "sitzbaths," halfbaths, nightly moist compresses, etc. Of equal importance is training in proper breathing technique. This means preeminently diaphragmatic breathing, which all patients with the gastrocardiac syndrome first have to practise in prone position and later keep up in sitting or standing posture. Diaphragmatic breathing is identical with the abdominal type of respiration: The hands bear gently down on the abdomen so as to provide a certain degree of resistance; the abdomen is slowly expanded as much as possible, without at the same time expanding the thorax, and kept in this position for a short time; it is then drawn inward to the greatest possible extent. This exercise not only affects the diaphragm, but also to a certain extent the heart and aorta, as one may observe on fluoroscopic examination. The musculature both of the diaphragm and the abdominal walls is gradually strengthened and its innervation led back to normal function. Simultaneously the liver is squeezed out like a sponge, whereby the entire circulation within the abdominal cavity is regulated and improved and the conditions for absorption of intestinal gases bettered. Later on systematic and graded mountain climbing, gymnastics, swimming, etc., is prescribed whereby the confidence of the patient is increased and the gaseous distention of the abdomen reduced.

Carried out in this systematic manner and for a sufficient length of time, this therapy of gastrocardiac symptoms in patients with sound hearts yields splendid results in the great majority of cases. The lowering of the left diaphragmatic dome can well be noted with the fluoroscope. In these cases the heart needs no special treatment; in fact, it might only do physical harm. Perhaps, too, the transition from a gastrocardiac neurosis to a real arteriosclerosis can thus be prevented.

Our problem is much more complicated if the described syndrome is found in patients with organic heart disease, in particular arteriosclerosis. The differential diagnosis between a pseudoangina due to abnormal elevation of the diaphragm and a beginning sclerosis

of the coronary arteries, with or without cardiac insufficiency, is at times extremely difficult and places the physician before a most responsible decision. The difficulty is even greater if the patient is an inveterate smoker with a nicotin angina and smoker's gastritis.

The final decision depends first on the functional test of the circulatory apparatus. Further, the effect of nitrites is of importance: nitroglycerin acts quite promptly in the earlier stages of coronary sclerosis, but as a rule, has no effect on the gastrocardiac symptoms of patients with normal hearts. Finally, this last class of patients are usually able to take a walk immediately after a hearty meal, while those with organic heart lesions, as a rule, cannot do so without marked distress, even if the coronary sclerosis is in its incipiency.

As to treatment, the measures recommended for the purely functional gastrocardiac syndrome apply also to cardiac patients. In addition, each patient requires individualization as to exercise and rest, theobromin and other vasodilator remedies, nitrites, digitalis, balneotherapy, etc.

Psychically, it is wise to put the greater emphasis on the gastric and digestive disturbances when talking to such patients, so as to relieve their apprehension. As a matter of fact, the gastric treatment, the training of the diaphragm, the reduction of overweight, in short, the régime required in the treatment of the gastrocardiac neurosis, also exerts a favorable effect upon an organically affected heart because they reduce its load. Our therapy will be most successful if it takes into consideration not only the diseased organ, but also the interrelation between various organs. It is of such cases that Boadbent aptly says that "In practice the treatment of the stomach and nerves is more successful than treatment of the heart itself."

Summary. Attention is called to a group of cardiac symptoms which are produced by disturbances of the digestive tract, more particularly by an excessive accumulation of air in the stomach. This complex of symptoms for which the term "gastrocardiac syndrome" (gastric cardiopathy) is proposed, occurs most frequently in persons with a normal circulatory system. It is extremely annoying and often very alarming, and is apt to give rise to mistaken diagnoses of heart disease and inappropriate treatment. Organic cardiac lesions may, coincidentally, exist in patients with this gastrocardiac syndrome and complicate the latter condition considerably, but an exact differential diagnosis is not difficult. The proper treatment of gastric cardiopathy consists, in the main, of diet, certain drugs and physiotherapeutic procedures, and yields splendid results in the great majority of the cases.

AN ANALYSIS OF ONE HUNDRED EXAMPLES OF CARDIAC PAIN IN PRIVATE PRACTICE.*

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It is often supposed that the cardiologist has mainly to deal with chief complaints such as edema, dyspnea and palpitation. Such, however, is not the case. The most important chief complaint with which the cardiologist is concerned in private practice is cardiac pain. It seems that shortness of breath, as a rule the earliest manifestation of a gradually failing heart muscle, is not the complaint that brings the patient to him, but cardiac pain, Nature's other "danger signal," prompts the patient to seek medical advice.

This article summarizes the results obtained from a study in detail of 100 cases with a chief complaint of precordial pain. These patients were all ambulatory office patients, and only cases where cardiac pain was the primary complaint have been included. In this summary many of the details have been omitted and only a few of the most interesting results are presented. No attempt has been made to seek out any particular type of patient with a presenting symptom of cardiac pain. The patients were taken in consecutive order as the files of the office were consulted from February, 1927, to January, 1930. In order to obtain 100 cases with pain as a presenting symptom 401 cases had to be reviewed.

Incidence and Arbitrary Grouping. One is impressed by the high incidence of cardiac pain. Practically 25 per cent of all patients visiting our office have this as a primary complaint. Due consideration is taken, however, of the fact that we are dealing, for the most part, in our practice, with degenerative heart disease. To classify a group of people with this complaint immediately becomes very difficult, because it must be considered a symptom complex, and any arbitrary grouping will not be correct. For example, a case placed in the arteriosclerotic group may have suffered from a mild coronary episode, and the hypertensive may or may not have arteriosclerosis as an etiologic factor. Likewise, the patients grouped as angina pectoris with negative findings may be the victims of sclerotic changes in the coronary arteries. It is

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also possible that the coronary patient may well have been classified in the hypertensive group prior to occlusion. The following procedure has been adopted (Table 1*a*):

TABLE 1*a*.—INCIDENCE ACCORDING TO CLINICAL CLASSIFICATION.

Hypertensive	22
Arteriosclerotic	29
Syphilitic	2
Rheumatic	4
Thyroid	1
Coronary pathology	11
Angina pectoris	26
Obesity	1
Effort syndrome	4
Total	100

In the hypertensive group are placed patients whose records show no obvious coronary attack nor inordinate degree of arteriosclerosis upon examination of the peripheral vessels or of the eye grounds. A diastolic pressure of 100, or greater, has been used as an index.

The arteriosclerotic patients are usually of the sixth or seventh decade, with low blood pressure, where unmistakable coronary pathology could be excluded by history and whose symptoms were referable to a dying myocardium.

The rheumatic, syphilitic and thyroid classifications were made according to etiological evidence.

The patients in the angina pectoris group were between the ages of 35 and 55 years, the majority of whom showed negative findings in the physical examination, 2-meter Roentgen ray plate and electrocardiographic record. (The character and duration of the pain and absence of other symptoms were not characteristic of coronary disease.)

Patients have been selected for the coronary group according to a history of prolonged pain, abdominal symptoms, sweating and collapse, fever, leucocytosis and pericardial rub, or, in other words, the syndrome now recognized as coronary thrombosis.

The patient in the obesity group is believed to be suffering from endocrine dysfunction, and a favorable report has been received after pituitary therapy.

The effort-syndrome group includes 4 patients who show the usual manifestations of this condition, with cardiac pain as a prominent symptom.

Family History. Of the entire series 50 per cent gave a family history of cardiovascular disease, nephritis or diabetes. The hypertensive group showed a higher percentage of hereditary predisposition (Table 1*b*).

Occupation. Very rarely is a discussion of cardiac pain free from reference to incidence among physicians. Table 2 shows 5 per cent

of this class in the angina pectoris and coronary groups, and also gives confirmatory evidence of general knowledge of the high frequency of occurrence among brain workers. Due consideration, of course, must be given to the economic and social levels of an office clientele.

TABLE 1*b*.

	Cases.	Positive family history.	Percentage.
Hypertensive	22	14	64
Arteriosclerotic	29	13	45
Syphilitic	2	1	50
Rheumatic	4	2	50
Thyroid	1	1	100
Coronary	11	5	45
Angina pectoris	26	13	50
Obesity	1	1	100
Effort syndrome	4	0	0
Total	100	50	50

TABLE 2.

	Hypertensive.	Arteriosclerotic.	Syphilitic.	Rheumatic.	Thyroid.	Coronary.	Angina pectoris.	Obesity.	Effort syndrome.
Physician	3	1	..	..	..	2	3		
Housewife	8	5	..	1	1	1	4		
Merchant	3	4	1	..	..	1	4		
Manufacturing	3	3	..	1	..	1	3		
None	..	1	..	..	..	..	..	..	1
Publishing	..	..	..	..	..	..	2		
Real estate	..	2							
Clerk	..	..	..	1	..	..	4	..	1
Artisan	1	1	1	..	..	..	2	..	1
Clergyman	..	..	..	..	..	1			
Accountant	..	1	..	1					
Corporation executive	..	2	..	..	..	1			
Retired	2	2	..	..	..	..	1		
Lawyer	1	3	..	..	..	1			
Domestic service	..	2	..	..	..	..	..	1	
Teacher	..	2							
Tailor	..	..	..	..	..	1			
Broker	..	..	..	..	..	..	1		
Dentist	..	..	..	..	..	1			
Optometrist	..	..	..	..	..	1			
Agent	..	..	..	..	..	..	1		
Insurance	..	..	..	..	..	..	1		
Oysterman	1								

Age and Sex. No new facts have been determined in this part of the investigation. As one would expect, we find a slightly higher rate of occurrence among males in the hypertensive group; a higher percentage in the arteriosclerotic group; a striking predominance of the male sex in the coronary and angina pectoris divisions. We note the average age at the time of the first examination for the

hypertensive, arteriosclerotic and coronary groups, varying between 58.4 and 60.4 years, in contrast to the average of 48.8 years for the angina pectoris patients. (Table 3.)

TABLE 3.

	Male.	Female.	Average age at time of first examination.
Hypertensive	12	10	60.4
Arteriosclerotic	21	8	58.4
Syphilitic	2	..	44.0
Rheumatic	2	2	30.5
Thyroid	..	1	47.0
Coronary	10	1	59.7
Angina pectoris	23	3	48.8
Obesity	..	1	58.0
Effort syndrome	3	1	33.5

Analysis of Pain and Secondary Complaints. We find exertion as an exciting cause occurring in numerical proportion in all groups. Dyspnea as a secondary symptom is noted only in 6 of the angina pectoris group. Four of the entire number of cases manifested apprehension—fear of impending death—and it is of interest to find 3 classed in the functional angina pectoris division and the remaining 1 as coronary. Three of the 4 rheumatic cases, all suffering with mitral disease, showed constant pain which we believe to be of fatigue origin. The absence of aortic-valve involvement in this very small group of cardiac rheumatics is contrary to general observation, and is considered worthy of mention. Over 50 per cent of the coronary group also suffered with constant pain. This high percentage is outstanding as compared with the other clinical varieties of degenerative heart disease. Vertigo as a secondary symptom more frequently complicated cardiac pain among the arterioslerotics. (Table 4.)

TABLE 4.

	Character.					Exciting cause.			Secondary symptoms.			
	Constant.	Paroxysmal.	Dull pressure.	Stabbing, burning or choking.	Radiation to arms, jaw or shoulders.	Exertion.	Meals.	Exposure to cold or wind.	Dyspnea.	Vertigo.	Nausea or vomiting.	Apprehension.
Hypertensive	5	16	2	1	12	15	1	..	8	1	2	
Arteriosclerotic	2	22	7	5	13	19	4	2	9	4		
Syphilitic	..	2	1									
Rheumatic	3	1	..	2	1	2	..	..	2			
Thyroid	1	..	..	1								
Coronary	7	4	..	2	6	5	1	..	2	1	1	1
Angina pectoris	3	17	3	4	8	12	..	2	6	1	3	3
Obesity	1	..	1									
Effort syndrome	2	2	..	1	..	2	..	..	..	1		

Clinical Course of Groups. This information was obtained from ordinary clinical conservation in office practice and by means of replies obtained from a questionnaire sent to patient, friend, or physician. The hypertensive cases show the highest mortality with no patient symptom-free, and very few classed as improved. The arteriosclerotic has the lowest group mortality rate and a very satisfactory number classed as improved. While no coronary patient may be classed as symptom-free, the living patients could be grouped as unchanged or improved. Nearly 50 per cent of the total angina pectoris patients were improved, and in addition 4 reported as being symptom-free. (Table 5.)

TABLE 5.

	Died.	Group mortality, per cent.	Worse.	Unchanged.	Improved.	Symptom-free.	No information available.
Hypertensive	9	41	2	3	5	..	3
Arteriosclerotic	3	10	1	4	14	1	6
Syphilitic	..	..	..	1	1		
Rheumatic	..	..	..	..	3	..	1
Thyroid	..	..	..	..	1		
Coronary	4	36	..	3	4		
Angina pectoris	4	15	..	2	12	4	4
Obesity	..	..	..	..	1		
Effort syndrome	..	..	1	1	1	..	1

Electrocardiographic Study. In reviewing the electrocardiographic findings several interesting features may be noted. Forty per cent of the angina pectoris group showed no abnormality. The 4 effort syndrome patients, as would be expected, gave evidence of somatic tremor, otherwise negative. Two of the 3 cases of auricular fibrillation are found in the rheumatic group. There was a relatively high incidence of ectopic ventricular contractions among the arteriosclerotic patients, these 29 patients presenting this disturbance in greater number than was observed among the remaining 71. More than 33 per cent of the coronary cases showed a negative *T* wave in the first lead. "Pardee's sign" (convex *S–T* interval) was found in one instance. Among the 11 no record in this group could be classified as "normal mechanism, no evidence of cardiac pathology." (Table 6.)

Electrocardiographic Study of Fatal Cases. In this analysis we observe serious changes in the graphic records of all groups, with the exception of the angina pectoris class, where 2 out of 4 patients showed no abnormality of a grave nature. Eleven out of 20 manifested depression or negativity of the Lead I *T* waves. Pardee's sign is noted as present in 1 of the arteriosclerotic groups. (Table 7.)

TABLE 6.—ELECTROCARDIOGRAPHIC FINDINGS.

	Hypertensive.	Arteriosclerotic.	Syphilitic.	Rheumatic.	Thyroid.	Coronary.	Angina pectoris.	Obesity.	Effort syndrome.
Left axis deviation	13	20	..	1	..	6	8	1	
Right axis deviation	1	..	..	1					
Intraventricular block	1	2							
Right bundle-branch block	1	2	1						
Auricular fibrillation	..	1	..	2					
Ectopic auricular contractions	2	2	..	..	..	2			
Ectopic ventricular contractions	1	6	..	..	..	2	1		
Prolonged auriculoventricular conduction	2	5	..	..	..	1	4		
Sinoauricular block	..	..	..	..	..	..	1		
Sinus bradycardia	..	..	..	..	..	..	1		
Partial heart block (2:1)	..	..	..	..	..	..	1		
Negative *T* wave, Lead I	4	4	..	..	..	3			
Negative *T* wave, Leads I and II	1	1	..	1	..	..	2		
Negative *T* wave, Leads I, II and III	..	1							
Negative *T* wave, Leads II and III	2	..	1	..	..	..	1		
Depressed *T* wave, Leads I and II	2	3	..	..	..	2	1		
Q–R–S low voltage	2	..	..	1	..	2	1		
Q–R–S marked notching or slurring	6	5	..	..	..	3	4		
Prominent *Q* waves	3	2	..	..	1	2	3		
Convex *R–T* interval	..	1	..	..	..	1	1		
Negative findings	1	1	..	1	..	..	10	..	4

TABLE 7.—RECORDS OF TWENTY FATAL CASES.

Records.	Clinical class.	Positive electrocardiographic findings.
IISF	Hypertensive	Left axis deviation; notched *Q–R–S; T*, I and II diphasic.
IIPD	Hypertensive	Left axis deviation; *T*, I negative.
ISBD	Hypertensive	Left axis deviation; *T*, I and II negative.
IOFF	Hypertensive	Left axis deviation; *T*, I negative; deep *Q*, I.
IOSL	Hypertensive	Left axis deviation; aur.-vent. conduction (20); *Q*, I present.
IILI	Hypertensive	Left axis deviation; *T*, I negative.
IHLF	Hypertensive	Right branch block.
IBFF	Hypertensive	Left axis deviation; aur.-vent. conduction (24); ectopic vent. beats.
IBOH	Hypertensive	*T*, I negative; *Q–R–S*, slurred; extremely low voltage.
IIPO	Angina pectoris	Left axis deviation; otherwise negative.
IHLL	Angina pectoris	Deep *Q*, II; otherwise negative.
ISFL	Angina pectoris	Prolonged aur.-vent. conduction (24); slurred *R*, II upstroke.
IBDH	Angina pectoris	Left axis deviation; *T*, I and II negative.
IHBL	Coronary	*T*, I negative; slurring of ventricular spikes.
IHHD	Coronary	*T* waves, isoelectric; slurring of ventricular spikes.
IHLD	Coronary	Left axis deviation; *Q–R–S* slurred; low-voltage; ectopic vent. beats.
IOFS	Coronary	Left axis deviation; *T* waves, isoelectric.
IBFF	Arteriosclerosis	Intraventricular block (*Q–R–S* 14).
IBFP	Arteriosclerosis	Left axis deviation; auricular fibrillation; ectopic vent. beats.
IBIH	Arteriosclerosis	Left axis deviation; *T*, II and III negative; slurred, notched *Q–R–S*; *S–T*, convex.

Summary and Conclusions. 1. The patient seeks advice of the cardiologist mainly on account of cardiac pain.

2. Over a 3-year period 401 cases occurring in office practice were reviewed, of whom 100 presented cardiac pain as the prominent symptom.

3. The patients were grouped arbitrarily as follows: hypertensive, arteriosclerotic, rheumatic, syphilitic, thyroid, angina pectoris, obesity, effort syndrome.

4. Exertion appeared most frequently as an exciting cause in all groups.

5. Highest mortality occurred in the hypertensive group and the lowest in the arteriosclerotic group.

RHEUMATIC FEVER IN ADULT PORTO RICAN IMMIGRANTS.

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The different character and course of rheumatic infection in children and adults have been repeatedly emphasized in recent years. Ehrström[1] and Swift in particular have pointed out the analogy between tuberculosis and rheumatic fever: "the fact that in both tuberculosis and rheumatic fever severe general acute manifestations are more frequent in the young than in the old. In succeeding decades of life there is a transition from generalized manifestations to more localized lesions."[2] It is believed that this difference is determined by the development of an allergy to the infectious agent. This allergy in the adult may be brought about, not alone by earlier frank rheumatic infections, but very possibly by repeated exposures to the virus, which give rise to no clinical evidences of the disease. According to this view, the adult reacts differently than does the child to rheumatic infection because previous contact with the virus of the disease has altered his tissue and humoral reaction to its invasion. The ubiquity of rheumatic infection in temperate climates explains the typical adult reaction to rheumatic infection.

Many instances are on record of the increased invasiveness and the fulminating character of various infectious diseases striking for the first time a nonimmune adult population. The malignancy of measles affecting an isolated community of Samoan natives has often been cited.[3] The Senegalese when brought to France during the World War were affected in great numbers with an acute progressive form of generalized tuberculosis.[4]

Recently I observed what seems to be an analogue, a severe infection with rheumatic fever in a Porto Rican adult. The idea suggested itself that perhaps this increased virulence of the disease might be explained by the absence of rheumatic infection in Porto Rico, resulting in a greater susceptibility of Porto Ricans on exposure to the disease in the United States where rheumatic fever is endemic. This paper represents an attempt to test the validity of this assumption.

Accordingly all of the hospital records of the past three years of Porto Ricans with rheumatic fever or rheumatic heart disease, as well as 100 charts of the past three years, selected at random, of non-Porto Ricans who were treated for the same conditions were studied. Of the non-Porto Ricans, who for the sake of brevity will be referred to as "controls," 43 were American born and 51 were foreign born. Most of the foreign-born came from Russia and Central Europe where rheumatic fever is endemic. Included with the Porto Ricans are 3 from the British West Indies, 1 from the Virgin Islands, 1 from Venezuela, and 1 from South Carolina. Only patients fifteen years and older were included in the study.

TABLE I.—RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE IN PORTO RICANS AND CONTROLS.

	Controls.		Porto Ricans.	
Number of cases:				
Males	36		9	
Females	64		9	
Total	—	100	—	18
Average age, years		32.0		26.6
Number of foreign born		57		18
Average age on immigration		21.0		19.8
Average age at first infection		16.5		22.6
Patients admitted for rheumatic fever:				
Number		35		13
Average age		29.8		24.5
Patients admitted for cardiac insufficiency:				
Number		43		2
Average age		37.5		28.0
Patients admitted for miscellaneous conditions:				
Number		22		3
Average age		29.0		35.0
Number with cardiac lesions and no history of infection		20		1
Number with history of chorea		9		0

Tables I and II summarize the findings in the two series. The controls were on the average five years older than the Porto Ricans, and the foreign born among them, on their arrival in the United States, were on the average one year older than the Porto Ricans were at the time of their immigration. Striking is the fact that not one of the Porto Ricans gave a history of rheumatic infection before coming to this country. Their average age at the time of immigration was 19.8 years, while the average age on the occasion of the first rheumatic infection was 22.6 years. This contrasts

with an average age at the time of first infection of 16.5 years for the controls. Almost one-half of the foreign born controls had had their original infection in the country of their birth. A number of the Porto Ricans contracted their infection very soon after arriving in New York City. Only two of the Porto Ricans were admitted to the hospital because of cardiac failure, whereas nearly one-half of the controls sought treatment for cardiac insufficiency. Porto Rican immigration has been very active for only a few years, and since valvular disease develops only after their arrival in this country, the time has been too short for the evolution of advanced valvular lesions.

TABLE II.—CASES OF ACTIVE RHEUMATIC FEVER.

	Controls.	Porto Ricans.
Number of cases	35	13
Average age, years	29.8	24.5
Duration, weeks	7.4	9.8
Number with pericarditis	6	5
Number with violent onset	1	6
Number with nodules	1	1
Number in whom severity of disease was:		
Mild	9	2
Moderate	15	2
Severe	11	9
Deaths	5	3

Three quarters of the Porto Ricans were admitted to the hospital for some manifestation of acute rheumatic fever, whereas only one-third of the controls sought hospital care for this reason. The average age of these Porto Ricans was 24.5 years, and of the controls with acute febrile episodes 29.8 years. This difference of five years in the ages of the two series hardly seems great enough to account for differences in the severity of infection, yet for the most part, the disease was more acute, more prolonged, and more protean in its manifestations in the Porto Ricans. The severity of an infection by an unknown virus is difficult to judge objectively, but certain data are helpful. The duration of the bout of rheumatic fever for which the several patients were admitted was on the average 9.8 weeks in the Porto Ricans, and 7.4 weeks in the controls. Five, or 38 per cent of the Porto Ricans developed pericarditis, whereas only 6 or 17 per cent of the active cases of rheumatic fever among the controls had pericardial involvement. Six of the 13 Porto Ricans had a dramatic onset of the disease with chills, or with epigastric pain and vomiting; only two of the 25 controls, had such a stormy onset. It is interesting that none of the Porto Ricans had had chorea nor were seen with chorea, whereas 9 of the controls had histories of chorea. One adult Porto Rican and 1 control exhibited rheumatic nodules. Three Porto Ricans and 5 controls died from their infection.

An attempt was made to classify the severity of the infection in each case. Criteria were the violence of onset, the duration, the variety and extent of the clinical manifestations, and the gravity of the cardiac infection. Among the Porto Ricans 2 cases were mild, 2 were moderately severe and 9 were severe; among the controls 9 cases were mild, 15 were moderately severe, and 11 were severe, judged by these criteria. In both groups the average duration of the mild cases was four weeks, of the moderately severe cases seven weeks, and of the severe cases 11.7 weeks for the Porto Ricans and 9.6 for the controls. Neither the ages of the subjects nor the number of previous manifest rheumatic infections which they had experienced influenced the severity of the attacks. Indeed in the present control series the average age of the patients with the graver form of the disease was greater than that of those with the mild form.

Among North American and European patients with rheumatic heart disease one finds many who give no history of previous acute rheumatic episodes. These patients apparently have been subjected to a low grade chronic "subclinical" infection. Yet among the Porto Ricans of my series only one subject fell into this group and she had been in the United States for nine years when first observed. This is added evidence of the rarity of rheumatic fever in Porto Rico, and of the severity of the infection once it attacks a Porto Rican.

Twelve additional cases of rheumatic heart disease in Porto Ricans were found in the records of the cardiac clinic of the past three and a half years. Their average age was 24.4 years, their average age on immigration 18.5 years, and at the time of their first rheumatic infection 20.4 years. With one exception they were patients with early valvular lesions and no history of congestive heart failure. Seven of them exhibited only mitral insufficiency contracted after their arrival in the United States following mild attacks of fever and arthritis. Only one of this group had had a severe rheumatic infection. Two of the dispensary patients had definitely had rheumatic fever with cardiac involvement while in Porto Rico. One a girl, aged eighteen years, had had torticollis at the age of ten, and joint pains at the age of eighteen just before coming to the United States. Five months after her arrival she had mitral stenosis and insufficiency. The second patient, a man aged twenty years, had been ill with arthritis for six months at the age of fifteen while in Porto Rico. Two months after his arrival in the United States at the age of twenty the existence of a mitral stenosis was established. One Porto Rican girl of the dispensary group had chorea four years after coming to the United States.

The individual histories are more convincing than such statistical summaries on a small number of cases. The first case is the one that first drew my attention to the problem.

Case Reports. CASE I.—Hospital No. 316789, a Porto Rican male, aged twenty years, who came to New York City at the age of seventeen years, was admitted to Mt. Sinai Hospital on July 24, 1930. He had had no previous attacks of arthritis, tonsillitis or chorea. Five months before he had had sudden pain, redness and tenderness of both ankles and the right wrist. This lasted for four days. He then had a free interval of two or three days which was followed by a recurrence of the arthritis which again lasted a few days. Ever since then he has had repeated attacks of arthritis lasting a few days followed by a free interval of a few days. In these bouts the shoulder joints, the ankles, the tarsal joints, the knees, the wrists were successively or simultaneously involved. During the attacks he always had fever and at times true chills. Four days before admission there again was recurrence with fever and inflammation of the left knee, wrist, both ankles and the left shoulder. For three and a half months the patient had experienced dyspnea and palpitation on exertion, and in the outpatient department heart disease had been diagnosed.

Examination on admission revealed an acutely ill patient, with a temperature of 104°, a pulse of 112 and painful inflammation of both shoulders, the left sternoclavicular joint, the left wrist, both knees and ankles and the small joints of the left hand and of the feet. The heart was somewhat enlarged to the left and right. Presystolic and systolic murmurs were heard at the apex and a diastolic murmur along the left sternal margin. The white cell count totalled 17,500 with 77 per cent polymorphonuclears and 23 per cent mononuclears. The hemoglobin was 76 per cent. On the third day, as a result of active salicylate therapy, the temperature was normal and the joint inflammation had subsided. Coupled premature beats were heard. On August 4 the knuckles of the left hand and the knees were again painful; the heart rate was 108. On August 7 the hemoglobin was 75 per cent. On August 8 when the administration of salicylates had been stopped there again was pain in the left shoulder and the temperature rose to 100°. On August 18 he had been afebrile for one week. On the following day the proximal interphalangeal joint of the left index finger became swollen and painful, but subsided in a few days. The temperature during the first week ranged from 98° to 104.4°, during the second from 98.6° to 100°, the third from 98.6° to 101.2° and during the fourth was normal. Although the boy was soon afterward discharged, it is doubtful whether he was rid of his infection. Electrocardiograms during the course of infection showed prolongation of the P–R interval to 0.33 second and changes in the S–T segment.

Summary. A patient with a continuous infection for over six months, with repeated bouts of arthritis involving at various times a great number of joints, including many of the small joints. On admission there was a high leukocytosis. An active myocarditis was evidenced by electrocardiographic changes and a persistently rapid heart rate.

CASE II.—Hospital No. 311954, a Porto Rican, male, aged twenty-six years, was admitted to the hospital on March 5, 1930. He had had no attacks of arthritis, chorea or sore throat while in Porto Rico. He came to the United States at the age of twenty-three years. At the age of twenty-four years he had pain and swelling of both ankles, which lasted two months. Three weeks before his admission he became febrile and experienced severe pain and swelling of both knees. This was followed by pain in the toes, fingers and the left shoulder. On admission he appeared acutely ill, with severe pain and acute arthritis in the left knee and in the toes of the right foot and the interphalangeal joints of the right hand. The heart was slightly enlarged to the right. A short soft apical systolic murmur and a faint diastolic murmur to the left of the sternum were

audible. The white blood cells totalled 12,300, with 62 per cent polymorphonuclear cells. The hemoglobin was 92 per cent. The temperature during the first week ranged from 101° to 104°, during the second and third from 99° to 101.5°, the fourth from 98.6° to 101° and after this was normal. A few days after admission both knees and the left shoulder were involved. The following day a pericardial friction rub became audible. Then the right wrist became inflamed, a week later the left metacarpophalangeal joints, the next day both wrists. The pericarditis persisted, and on March 27 underwent an acute exacerbation. Electrocardiograms, taken at intervals during the infection showed on March 17 abnormal *R–T* transitions in Leads I and II, and on several occasions inverted *T* waves in Leads II and III. On April 4 the temperature finally became normal and the symptoms subsided. The patient was seen again on May 26, some weeks after his discharge from the hospital. By this time he had developed auricular fibrillation, although his valvular defects were not far advanced.

Summary. A young man with acute arthritis, pancarditis, and a febrile course of seven weeks, who during convalescence developed auricular fibrillation.

CASE III.—Hospital No. 302133, a negress from the British West Indies, aged twenty-nine years, who had come to the United States at the age of eighteen years. During her twenty-sixth year she was ill for the whole year with joint pains. Then a tonsillectomy was performed. Before this she had had frequent sore throats. She was admitted to the hospital on May 4, 1929, at the age of twenty-nine years. Two weeks previously she had had a chill which was followed by a sore throat and pains in all the joints, with swelling of the fingers of both hands. The pains gradually subsided but the fever continued. For three days preceding her admission she had had sticking pains in the left chest anteriorly and profuse sweats. Examination revealed an acutely ill woman. There was no swelling of any joints, but the elbows were painful on motion. The heart was enlarged to the left and right and a presystolic thrill and murmur were present at the apex. The pulmonic second sound was accentuated. The hemoglobin was 60 per cent; the white cells totalled 15,300, with 82 per cent polymorphonuclears and 18 per cent mononuclears. On May 11 acute pericarditis developed; on May 18 there was pain in the left knee. On May 31 the white cell count was still high—11,900, with 64 per cent polymorphonuclears, 34 per cent mononuclears and 2 per cent eosinophils. On June 12 the hemoglobin was 50 per cent. On June 21 a newly developed aortic diastolic murmur became audible. On June 30 many subcutaneous nodules appeared on the scalp, the elbows and the knees. By July 17 she was much better and was allowed out of bed. A few days later, however, there was a new rise in temperature and a fresh crop of rheumatic nodules appeared. During her whole stay in the hospital for twelve weeks her temperature ranged from 99° to 103.2°. It never remained normal more than a day or two, and was still elevated when she insisted upon leaving. On several occasions electrocardiograms showed prolongation of the *P–R* interval to 0.22 and 0.24 second, the last time just before her discharge, fourteen weeks after the onset of her illness.

Summary. A woman, the onset of whose illness was marked by a chill and sore throat, which was followed by arthritis and pericarditis and aortic valvulitis. Ten weeks later a crop of subcutaneous nodules appeared and after three more weeks a second crop. The fever lasted fourteen weeks and had not returned to normal when the patient escaped from observation.

Rheumatic fever is primarily a disease of the temperate zone. In the tropics it is much less common.[5,6,7] Indeed, in the southern United States the incidence of rheumatic fever is very low and it becomes rarer the further south one goes.[8,9] Dr. Pedro N. Ortiz, Commissioner of Health of Porto Rico, kindly supplied me with the following data on the crude death rate from rheumatic fever in Porto Rico.

DEATHS AND DEATH RATES PER 100,000 POPULATION, FROM RHEUMATIC FEVER IN PORTO RICO.

Fiscal year.	Deaths.	Death rates.
1925 to 1926	13	0.9
1926 to 1927	19	1.0
1927 to 1928	11	0.7
1928 to 1929	22	1.0
1929 to 1930	14	0.9

This compares with a crude death rate of 3 per 100,000 for the United States Registration area. Of the 22 deaths recorded for the year 1928–1929, 14 occurred in coastal towns, and 8 in the mountains of the interior.[10] Coburn[11] has gathered data showing that rheumatic fever is very rare in Porto Rico, but that occasional cases are encountered. Among 225 consecutive necropsies at the school of Tropical Medicine at San Juan no cases of acute or chronic rheumatic lesions of the heart were encountered.[12] In New York City and Boston the lesions of mitral stenosis are found in about 4 per cent of all necropsies. In New Orleans, however, the incidence is only 0.23 per cent.[7] These figures suggest that very possibly many of the deaths in Porto Rico attributed to acute rheumatic fever were due not to this disease but to some other condition. The classification of deaths as directly due to rheumatic fever is notoriously difficult and uncertain.

A somewhat conflicting statement appears in the report of the Surgeon General of the United States Army.[13] The annual admission rate per 1000 officers and enlisted men, for rheumatic fever among Porto Rican soldiers stationed in Porto Rico was 0.91 in 1926, and 1.63 in 1927, whereas the admission rate for white soldiers stationed in the United States was 0.65 in 1926 and 0.69 in 1927.

Of the 30 Porto Ricans with rheumatic fever and rheumatic heart disease whose records I have studied 2 gave histories of rheumatic infections before reaching the United States.

There are indications that negroes from the southern United States, who migrate to the North, react to rheumatic fever in much the same manner as do Porto Ricans. I have observed a case of severe rheumatic fever in a young negress from South Carolina, contracted shortly after her arrival in New York. Dr. John R. Paul informs me that from his studies in Philadelphia he has gained the impres-

sion that rheumatic fever in negroes recently arrived from the south runs an unusually severe course.

The data show clearly that rheumatic fever is rare in Porto Rico, and that the Porto Ricans who were observed while at Mt. Sinai Hospital contracted their infection after their arrival in the United States. This accounts for their more advanced age (22.6 years) at the time of their first infection.

Two further propositions are more difficult of proof: does rheumatic fever run a more severe course in Porto Rican immigrants; is this severer infection due to a greater susceptibility owing to lack of previous exposure in their native country?

Of course many individual cases of rheumatic fever of great severity are seen in adult native Americans. The distinguishing feature is that such cases among the native American population are the exception, among the Porto Ricans they are the rule. It is significant that, in 9 of the 13 Porto Ricans the disease was severe, that in the whole group the average duration of the febrile period was longer, and the incidence of pericarditis and the frequency of a stormy onset greater.

To explain why rheumatic fever in Porto Rican immigrants takes on a more fulminating form, certain analogies to the behavior of other infectious diseases attacking a nonimmune population have been pointed out. The thought will at once arise, why, if Porto Ricans lack immunity, do so few of them contract rheumatic fever when they come to the United States? One might imagine that the disease might assume true epidemic proportions among them. As a matter of fact the evidence that I have been able to gather suggests that rheumatic fever is uncommon among Porto Ricans in New York City. Mt. Sinai Hospital, because of its location near a large Porto Rican settlement attracts large numbers of Porto Rican patients, yet the number of rheumatics is few. The hospital statistics are confirmed by those of the dispensary. In the cardiac clinic from January 1, 1927, to September 1, 1930, only 33 Porto Ricans were admitted out of a total number of 936 new patients. Of these only 16 had rheumatic heart disease. The tuberculosis clinic of the hospital, on the other hand, reports that almost one-half of its patients are Porto Ricans.

Diseases vary in their degree of contagiousness, some such as measles attack practically every exposed nonimmune, others, and with these one must group rheumatic fever, are more highly selective in their distribution. The epidemics of rheumatic fever that have been described are characterized by a very slow diffusion of the contagion, and a rather limited extent.[7,14] It may be that massive doses of the virus are necessary for infection to take place. An analogy is offered by the course of development of tuberculosis in Senegalese troups in France, already quoted. Only a fraction

of the soldiers contracted tuberculosis, but those who became infected had a very severe form of the disease. The nature of rheumatic fever is apparently such that it never gives rise to explosive, widespread outbreaks. A second factor limiting the spread of the disease may be the fact that the Porto Ricans in New York live a rather segregated life and do not mingle much with other peoples.

It is not climate alone that determines the varying susceptibility of different peoples to rheumatic infection. It has been shown that the morbidity from rheumatic fever in the same locality varies with the different races. Thus the French experience with their troops in Morocco is shown in the following table taken from Andrieu:

MORBIDITY OF ARTICULAR RHEUMATISM PER 1000.

	Years.					
	1908.	1909.	1910.	1911.	1912.	1913.
Senegalese . . .	5.20	17.98	18.71	16.29	14.47	8.23
Europeans . . .	15.96	11.40	6.44	15.15	11.05	6.44
Indigenous Arabs .	8.41	4.73	2.30	3.19	3.37	2.95

The Porto Ricans in New York, as well as in their native island, are very poor, and their living conditions are for the most part indescribably bad. Most of them have intestinal parasites, and syphilis is very prevalent among them. It is possible that these factors serve to aggravate the severity of rheumatic infection when it occurs.

In some equatorial regions rheumatic fever is quite common. Thus together with its cardiac sequelæ it is prevalent in Cameroon and in Togo, yet in East Africa it is rare. It is frequent in the West Caroline Islands and in the Marshall Islands and in Tahiti, yet in Samoa it is almost unknown.[15]

Certain other diseases exhibit incomprehensible vagaries in the tropics. Scarlet fever is so rare in the tropics that one might imagine that the indigenous population, lacking acquired immunity, would be peculiarly susceptible to it. Yet, whenever it has been introduced in far southern latitudes only local small epidemics have resulted.[16] Studies by Otero[17] have shown that in Porto Rico the hemolytic streptococcus is encountered in cultures of normal throats far less frequently than in New York City. Both he and Pomales[18] found the same basal throat flora as in the United States, namely, Gram-negative cocci and nonhemolytic streptococci. Sore throats and tonsillitis are common among Porto Ricans on their native island. Pomales found hemolytic streptococci in 32 per cent of 50 Porto Ricans with acute tonsillitis, and hemolytic staphylococci in many. Yet, sore throats in Porto Rico are rarely followed by rheumatic fever. This is additional evidence that the relationship of tonsillar infection to rheumatic fever is not so close as has been supposed.

Summary. Rheumatic fever and rheumatic heart disease are very rare in Porto Rico. Rheumatic infection is not very common among Porto Ricans who have immigrated to New York City, but when infection does occur it is apt to be severe and in adults tends to approach the childhood type of the disease. This occurred in 9 of 13 cases of active rheumatic fever studied at Mt. Sinai Hospital. The cause of the varying incidence and severity of rheumatic fever in Porto Ricans and inhabitants of the temperate zone remains obscure. The data thus far available point to the desirability of a more intensive study of the semeiology of rheumatic fever, with particular reference to the prevalence of the disease, not alone in Porto Ricans, but in all parts of the world. At the same time a correlated study of the character and incidence of throat infections should be made. Such investigations might lead to a better understanding of the climatic factors as well as of the immune processes of the disease.

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THE CASE FOR AND AGAINST THE OPERATIVE TREATMENT OF ANGINA PECTORIS.

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All agree that the surgical treatment of angina pectoris is palliative only. Relief of pain, however, is always important, not only from the standpoint of the suffering of the patient, but also because, as suggested by Wenckebach and Daniélopolu, the pain in itself may actually be injurious to the organism. It is apparently the consensus of opinion at present that operation for angina pectoris should be reserved for the more severe cases. Of our cases of angina pectoris we deemed only one severe enough to warrant the use of surgical procedures. Our experience, however, with this case was so unique that we were stimulated to study the subject of the operative treatment of angina pectoris more carefully. The following is a brief report of our case.

Case Report.—The patient, an asbestos worker, aged fifty-five years, entered Georgetown University Hospital on May 23, 1929, giving a history of attacks of pain in the precordia over a period of two and a half months. At first the attacks had occurred only after exertion, but had become more frequent and more severe and finally began to appear when the patient was sitting quietly. During the preceding week they had been much more intense at night than in the day. The patient stated that the attacks lasted from one-half to one hour and that during them "the heart felt as if it was being torn out of the chest." The pain passed across the chest, down into the abdomen, up into the neck and down the left arm. For about a year there had been mild dyspnea on exertion.

Physical examination was essentially negative. A third heart sound was heard and seemed to be presystolic in time. The blood pressure was 98 systolic and 62 diastolic. The pulse rate varied from 80 to 100. A roentgenogram of the chest revealed nothing abnormal. The urinalysis was essentially negative. The hemoglobin was 62 per cent (Dare), the erythrocytes numbered 3,160,000 per c.mm. and the leukocytes 7900, of which 81 per cent were polymorphonuclear neutrophils. The Wassermann and Kahn tests of the blood were negative. The electrocardiogram showed regular rhythm, rate 100, sinus tachycardia, conduction time 0.2 sec. The only change in the electrocardiogram was the gradual development of left axis deviation as time went on.

During ten days in hospital the pain was relieved promptly but only for a short time by tablets of $\frac{1}{100}$ grain of nitroglycerin under the tongue. Ten to fifteen of these were required nightly but even then the patient had little rest.

On June 15 novocain with alcohol was injected into the first six left thoracic nerves paravertebrally by Dr. John Shugrue. On this day he had

one severe attack of pain but during the following three days was completely relieved. After this, however, the pain recurred and was as bad as before. In addition there were now some painful paresthesias over the left chest and inner side of the left arm.

On July 8, the left superior cervical sympathetic ganglion was removed by Dr. Shugrue under nitrous oxid, oxygen and ether anesthesia. During the next two weeks of convalescence in hospital there was almost complete freedom from pain. Soon, however, the patient began to complain of some pain in the left mandible and discomfort in the left axilla.

Shortly after leaving the hospital he began to experience great pain in the left jaw upon chewing, so much so that eating was an agonizing process, and his nutrition suffered accordingly. There were occasional attacks of precordial oppression, but no real pain.

In September the patient began also to complain of pain in the shoulders, especially the right. This pain gradually became more severe until it was present almost constantly and was excruciating. The muscles of both arms, especially the right, became markedly atrophic, and there was great limitation of motion at the right shoulder joint and some of the left. Roentgenograms revealed no abnormality of the shoulder joints, but the bones showed rarefaction. A careful neurologic examination was negative, except for Horner's syndrome on the left. It was thought that the patient might have a periarthritis of the shoulder joints with atrophy of disuse, and diathermy treatment was instituted. The possibility of transferred anginal pain was also considered. The pain in the jaw was attributed to a possible glossopharyngeal nerve involvement in the operative scar in the left side of the neck. The pain in the shoulders finally became so severe that there was no relief unless the patient was completely under the influence of morphin.

Two days before death he began to complain of dyspnea and showed slight pretibial edema. While pouring himself a cup of tea at supper time he suddenly died, November 25, 1929, eight and a half months after the onset of angina and four and a half months after the ganglionectomy.

Necropsy did not reveal any pathologic condition of the upper extremities. The arms were freely movable. There was bilateral hydrothorax. The heart weighed 455 gm. The coronary arteries were markedly sclerosed. The descending branch of the left coronary artery was apparently completely occluded by calcification, especially a short distance from its origin. There was some dilatation of the left ventricle, the apex of which was thin and bulging due probably to an old infarct. Evidence of fresh infarction was not found. There was moderate fibrosis of the myocardium.

In this case the patient would probably have been better off without his operation. His pain afterward was more severe, practically continual, more diffuse and the cause of great malnutrition. Pain in the jaw and face not infrequently follows this type of operation, and pains and annoying paresthesias of the chest and upper extremities are not uncommon. Naturally, if our treatment, which is aimed at relief of pain, itself is followed by other pain which may be just as severe, it is time to scrutinize that type of treatment to determine whether it is really worth while or whether it may not be improved upon.

We have collected and analyzed 138 cases of neurectomy for angina pectoris reported by forty-four various authors. (See Bibliography.) This is not a complete collection of recorded cases,

but we felt it to be sufficiently representative for our purpose. Before discussing this series of cases it would be well to make an inventory of our knowledge of the anatomy and physiology of the innervation of the heart and aorta and to discuss the nature of angina pectoris.

A summary of our knowledge concerning the innervation of the heart and aorta has been well given by Kuntz. A perusal of this shows how much there is yet to be learned on the subject. All of the nerves of the heart pass through the cardiac plexus which is situated at the base of the heart. These nerves are all sympathetc and vagal. The sympathetic nerves pass to and from the heart through synapses, mainly in the three cervical sympathetic ganglia, but also in the upper four or five thoracic ganglia. They are all apparently derived from the upper four or five thoracic spinal nerves. The efferent fibers accelerate and otherwise modify the heart beats doubtlessly by direct action upon the heart muscle. The afferent fibers (which pass through all of the sympathetic ganglia except the superior cervical) convey sensation, but also play some part in reflex vasomotor control. The vagal supply for the heart usually consists of three rami on each side. The fibers make synaptic connections in the cardiac plexus and also in ganglia in the heart itself. The efferent fibers are mainly inhibitory and exert their effect largely upon the sinoatrial node and the atrioventricular bundle. The afferent vagal impulses probably do not reach the threshold of consciousness, but elicit reflex vasomotor responses. The coronary arteries are supplied by both sympathetic and vagal fibers. The so-called depressor nerve is commonly regarded as a branch of the vagus, consisting mainly of afferent components which originate in the proximal parts of the aorta and adjacent cardiac wall. They exert their effect mainly upon the vasomotor and cardioinhibitory centers. This nerve is supposedly formed by a branch of the main trunk of the vagus which joins a branch of the superior laryngeal nerve. Surgeons apparently are not often certain of the location of this nerve.

Of all the theories of angina pectoris, that championed by Daniélopolu appeals to us as being most plausible. In brief, this theory is based upon the assumption of an inadequate coronary circulation, whether there is coronary sclerosis or an apparently normal heart. Angina pectoris is much more frequent when the coronary arteries are severely sclerosed than when they are healthy. The anginal attack arises from a disturbance of the balance between the work of the myocardium and its blood supply. Looked upon in this way, the theory can account for the occurrence of angina attacks in perfectly healthy young adults, since even healthy coronaries may be faced by an excessive demand. The theory also explains the many cases of coronary disease without anginal symptoms; in these it may be assumed that the occlusion has occurred

so slowly that sufficient anastomosis has had time to develop to maintain the balance. In the angina due to syphilitic aortitis partial and sometimes complete occlusion of the orifices of the coronary arteries in the root of the aorta is responsible for the condition. The objections to this theory, we believe, are less serious than to the aortic hypothesis put forward by Allbutt, Wenckebach and others. The hypothesis of spasm of the coronary arteries we hold to be untenable.

It must be emphasized, however, that there are other cardiac pains than those of true angina pectoris, particularly those accompanying acute aortitis and those associated with a failing heart. The subject of this paper is strictly limited to true angina pectoris as first described so accurately by Heberden. We are assuming that the cause of the pain arises in the heart, affects the afferent fibers of the sympathetic system concerned with sensation and is reflected as pain felt in the area of distribution of the peripheral nerves of the same segments as those from which the sympathetic nerves originate.

Franck (1899) was the first to suggest cervical sympathectomy for angina pectoris. Although the operation was done several times for various conditions, it was not until 1916 that Jonnesco performed the operation first for angina pectoris. C. H. Mayo has stated that he performed bilateral cervical sympathectomy for angina pectoris in 1913, but he has never published this report. Since 1916 many surgeons have recorded a few of these operations. Probably several hundred have been performed. The greatest activity in this direction seems to have occurred from 1923 to 1928. Recently one hears rather little of sympathectomy in connection with angina pectoris. Latterly, the alcoholic injection of the upper dorsal nerve roots has been advocated, of which more will be said later.

Various types of operations have been performed in the neck, with some success from each. The most complete type is that of Jonnesco, who resected the sympathetic chain with the superior, middle and inferior cervical ganglia and the first thoracic or stellate ganglion. Of the 138 case reports analyzed by us the types of operation were as follows:

1. Jonnesco type, unilateral, 21 cases (19 on left alone, 2 on right alone).
2. Jonnesco type, bilateral, 4 cases.
3. Removal of left superior cervical ganglion, 21 cases.
4. Removal of right superior cervical ganglion, 2 cases.
5. Removal of both superior cervical ganglia, 2 cases.
6. Division of sympathetic trunk below superior cervical ganglion and section of superior cardiac nerve, 3 cases.
7. Removal of the three left cervical ganglia, 11 cases.
8. Removal of the left superior and middle cervical ganglia, 12 cases.

9. Some combination of the above types, 15 cases.

10. Miscellaneous procedures on the sympathetic nerves of the neck, 35 cases.

11. Attempted section of the depressor nerve, 12 cases.

Of the 126 cases in which some one of the types of operation of the cervical sympathetic ganglia and nerves was performed complete relief of pain was reported in 50 (40 per cent), partial relief in 36 (29 per cent) and no relief in 34 (27 per cent). Results were not recorded in 6 cases. Of the 12 cases in which the cardiac depressor nerve or nerves were thought to be resected, complete relief was reported in 5 (41 per cent), partial relief in 3 (25 per cent) and no relief in 3 (25 per cent). The result was not recorded in 1 case.

Of all types, then, there was complete relief in 40.5 per cent of the cases, partial relief in 27 per cent and no relief in 26 per cent.

These results were apparently irrespective of the type of operation performed. The reason for relief is not apparent, because in no case were all of the afferent nerves resected. If we consider that the depressor nerves contain only fibers affecting the vasomotor and cardioinhibitory centers, and that the superior cervical ganglion has to do probably only with efferent fibers, it seems that all that is necessary is to break the cardiac nervous arc. Daniélopolu says that similar results from section of quite different nerves proves three things: "(1) That all these nerves contain sensory cardiac fibers; (2) that cutting some of the ascending fibers, without putting them all out of action, is sufficient to benefit angina; (3) that the abolition of the ascending nerve fibers (those passing to the cervical chain), having no possible relationship with the lateral group (those passing to the dorsal ganglia), nevertheless, prevent the occurrence of the pain syndrome of angina."

Wenckebach, in 1924, was of the opinion that section of the depressor nerve would prove to be the best operation, but these statistics show that it has no advantage over the other types of operation. Moreover, the operation is more difficult and less certain. His opinion was based upon the theory of the aortic origin of angina.

During the period of observation recorded 33 patients died. Of these 8 died during the operation or within a few hours, 7 lived from two to fourteen days, 4 died in from two weeks to a month, 10 died from one month to a year and 3 lived from one to three years (time of death not reported in 1, but was apparently soon after operation). The immediate operative mortality is probably about 6.5 per cent.

With complete relief, then, in 40.5 per cent of the cases and an operative mortality in such a serious disease of only about 6.5 per cent, the operative treatment of angina would seem to be a justifiable procedure. Since 7 of the cases dying apparently as a result of operation were instances of angina due doubtless to syphilitic aortitis (out of 28 such cases in the series) it appears that that type

of angina should not be treated in this way because of the risk, even though the results in the surviving cases were comparable to those of the whole series. Eliminating the cases of angina due to syphilitic aortitis, the immediate operative mortality becomes very low, namely, 1.8 per cent, which makes the procedure appear still more justifiable.

Further examination of our series of cases, however, reveals that there are other features which detract from the efficacy of this type of therapy. Of the 129 patients who survived the operation there were 40 (31 per cent) who had disagreeable or serious postoperative complications. In other words, not only was there only partial or no relief in 53 per cent, but in 31 per cent the patients were made less comfortable. These complications were largely of the nature of pains and paresthesias of variable duration, many of which were apparently permanent, as in our case. One of the commonest types of new pain was that of pain in the side of the face, jaw or neck. Some of these had severe pain when chewing. "Brachial neuralgia" was the next most frequently observed postoperative pain. Pain in the left shoulder was present in a few cases, and in 1 case the angina switched to the right side. In no case was there pain similar to that developing in our case. Paralysis of the vocal cords occurred in 2 cases. Some of these painful complications became less intense as time went on and a few apparently disappeared, but most of them persisted. We are willing to overlook the presence of Horner's syndrome because this is always to be expected after the Jonnesco operation.

Some of the patients in this series were observed for a brief period only after operation, while others were followed for years. The longest period of observation was twelve years (case of C. H. Mayo). It is impossible, of course, to determine exactly whether the operation had any effect upon the duration of the disease, but our impression is that the course of the disease was not materially affected. We have been very lenient in arriving at the percentage of deaths due to operation. No one can say whether a number of patients who died a few days or even a few weeks after operation may not have been hurried along to the end.

We may now summarize the case for and against the operative treatment of angina pectoris: The case for this type of treatment is: (1) Complete relief of the original pain in 40.5 per cent of cases and partial relief in 27 per cent; (2) low immediate operative mortality when cases associated with syphilitic aortitis are eliminated.

The case against the operative treatment of angina pectoris is: (1) No relief or only partial relief in 53 per cent of cases; (2) postoperative appearance of annoying paresthesias, new pains or other evil complications in 31 per cent of cases; (3) effectiveness of amyl nitrite or nitroglycerin for individual attacks of pain is certainly

much more than 40.5 per cent of cases; (4) apparent absence of influence upon the course of the disease.

A few words are now appropriate concerning the treatment of cardiac pains by injection methods. Brunn and Mandl, in 1924, tried paravertebral nerve block with procain, with excellent results. Recently Swetlow began the use of alcohol in these injections. Since his pioneer work others have used this method. The results have been much more constant than with the operative treatment, and the method has more to commend it scientifically, since the visceral afferent pain fibers must eventually pass through the rami communicantes and the dorsal roots regardless of the route up to that point. White has developed the most efficient method to date. He anesthetizes the upper five thoracic nerves as a routine with an injection of 5 cc. of 1 per cent solution of procain, followed by 5 cc. of 85 per cent alcohol. Relief from pain is usually prompt and may persist for several months. There is usually some hyperesthesia for about six weeks following the injection, but this is never as severe as the pains and painful paresthesias following sympathectomy. Furthermore, there is no operative mortality. Horner's syndrome usually follows, but this is of minor importance. Transference of pain to the epigastrium, however, has been noted.

Summary and Conclusions. 1. The anatomy and physiology of the innervation of the heart and aorta are summarized and found to be very incompletely known.

2. The most logical theory of angina pectoris is discussed; but this, like all other theories, is merely theory.

3. A specific case of the ill-effect of cervical sympathectomy for angina pectoris is cited, in which there was severe pain in the left jaw with chewing and transference of precordial pain to the shoulders.

4. The results of the operative treatment of angina pectoris in 138 cases collected from the literature are considered.

5. Whatever stand is taken regarding the subject, it is positive that the operative treatment should not be used for angina pectoris associated with syphilitic aortitis.

6. While the immediate operative mortality is very low, there is no evidence that the course of the disease is lengthened.

7. There is only partial relief of pain or no relief at all in 53 per cent of cases. Amyl nitrite and nitroglycerin certainly give relief from individual attacks in a much larger per cent of cases than are relieved by operation.

8. Annoying paresthesias or new pains follow operation in 31 per cent of cases.

9. Alcoholic injection of the upper thoracic posterior nerve roots gives relief for substantial periods of time and is apparently free of most of the ill-effects of operation. This method of treatment deserves a fair trial.

10. The operative treatment for angina pectoris at present should be performed only in selected cases and by neurosurgeons who wish to study carefully the anatomy and physiology of the innervation of the heart and aorta and the reasons for the post-operative complications. There is considerable information which can be learned in this way which cannot possibly be obtained from dissection of the human cadaver or experiments on living animals.

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A NEW AND SIMPLE MECHANICAL RETRACTOR FOR ABDOMINAL SURGERY.

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The successful execution of abdominal surgical procedures depends upon (1) the skill and judgment of the surgeon, and (2) adequate exposure. Of the former consideration we shall not deal here; to the latter consideration we shall devote this paper.

To maintain exposure of the abdominal viscera, the surgeon is required either to employ hand retractors manipulated by assistants, or mechanical retractors fixed in place and allowed to remain for the duration of the operation. There is no doubt that intelligent assistance with hand retractors is very helpful during the performance of difficult surgical procedures, yet many times the physical presence and hands of the assistant hamper the surgeon and obscure his view. On the other hand, a mechanically simple and efficient instrument for abdominal retraction relieves the assistant of duties and permits him to aid the surgeon in the actual intraäbdominal manipulations. He is free to hold important clamps and tissues, thus facilitating the operation.

During the past several years we have felt the need of a more efficient abdominal retractor than those which are in common use. We have employed several instruments which retract the abdominal incision from three places in a triangular manner. When this system is applied to an incision in the elastic abdominal wall it leaves a fourth side which is not restrained. The result is unbalanced forces, and it is this unbalanced system of forces which makes any three-point retraction of the abdominal wall or, for that matter any sphincter, inefficient and unsatisfactory.

We feel that an ideal instrument should retract from four dia-

metrically opposed places, and at the same time have no more than two of the retractors adjustable. These adjustable blades which, for convenience, we shall call the upper and lower angle blades, are used to retract the incision and also, by means of sterile gauze packs, to exclude viscera from the field of operation.

The conventional type of abdominal retractor has square corners which are prone to form obstruction when in use. In designing our instrument we made the side members curved (Fig. 5, *2* and *3*), so that the maximum space would be inclosed within a circular

FIG. 1.—Retractor frame. Bottom vue closed.

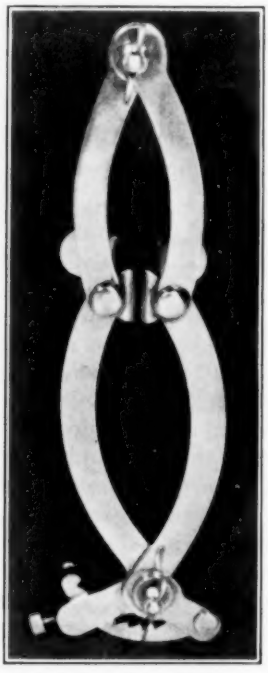

FIG. 2.—Retractor frame. Top vue closed.

opening, since, geometrically speaking, the circle embraces the maximum area for any given dimensions. The curved side members (Fig. 5, *2* and *3*) are levers united into one unit by very strongly riveted swivelled joints. The entire frame is securely held in place so that it cannot possibly slip by means of a ratchet catch and set screw at the lower angle (Fig. 5, *5*). The upper angle (Fig. 5, *1*) is also secured by pressure when the upper angle retractor is fastened. The side retractors are fixed permanently to the frame. Experience has shown that too many screws and adjustable parts complicate the instrument and are a source of annoyance. The

upper and lower angle retractors (Fig. 5, *1* and *4*) are detachable and slotted, and, therefore, adjustable to direct pull and a fair amount of lateral displacement. The blades are curved to restrain the incision and at the same time to hold in place deeper within the abdomen the sterile packs which restrain intruding organs which are not the subject of the particular operation.

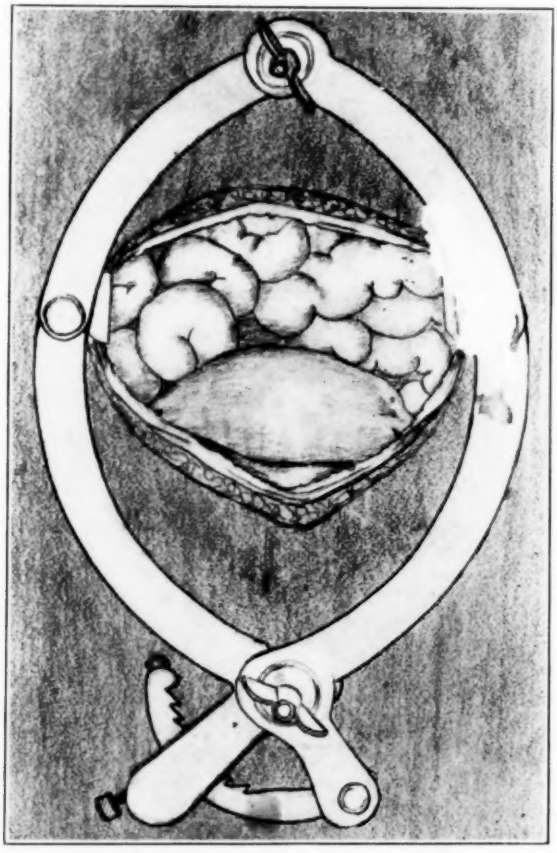

FIG. 3.—Hysterectomy. Lateral displacement of the abdominal wall by the curved side retractors the frame has been securely locked by the ratchet catch and setscrew.

So much for the technical details of this instrument. We shall now describe the modifications in abdominal technique, which Dr. O'Connor has devised for operative procedures with this instrument.

Lower Abdominal Procedures. *Hysterectomy, Salpingectomy.* The patient is prepared for operation in the usual routine manner.

A midline incision, about 8½ inches long, is made in the abdominal wall; the peritoneum is incised in the usual manner. The abdominal retractor is grasped in the right hand near the middle (Fig. 1), first one, then the other fixed side retractors are slipped into place. With both hands grasping the lower side members, the instrument is very quickly opened and then securely fastened by means of the

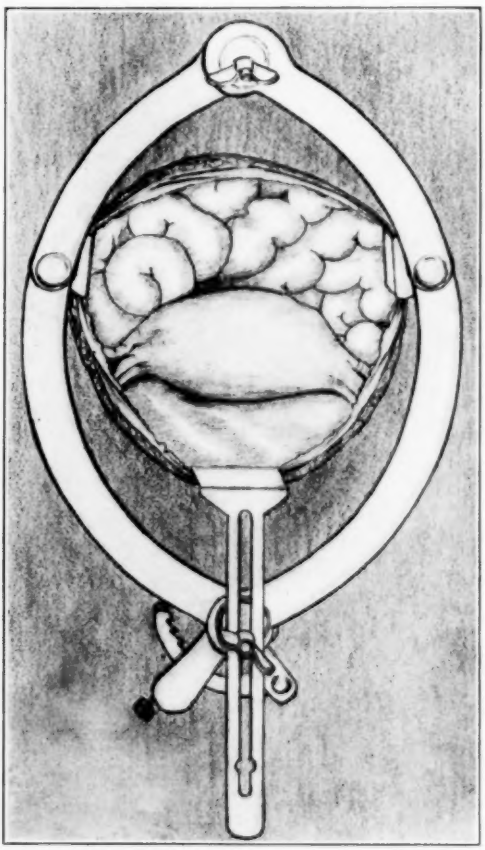

FIG. 4.—Hysterectomy. Lower angle retractor in place exposing bladder and uterus.

ratchet catch and set screw provided for that purpose (Fig. 3) at the lower angle. The patient is now placed in the Trendelenburg position, several gauze packs are slipped into the abdomen to exclude the viscera and the upper angle retractor is fastened in place with its blade restraining the packs and intestines. A thick piece of gauze, about 4 inches wide, is placed in the lower angle down to the level of the bladder and the lower angle retractor fixed in place.

With this exposure it is possible to perform quickly and with good vision the routine supravaginal hysterectomy or plastic procedures upon the tubes, ovaries or bladder.

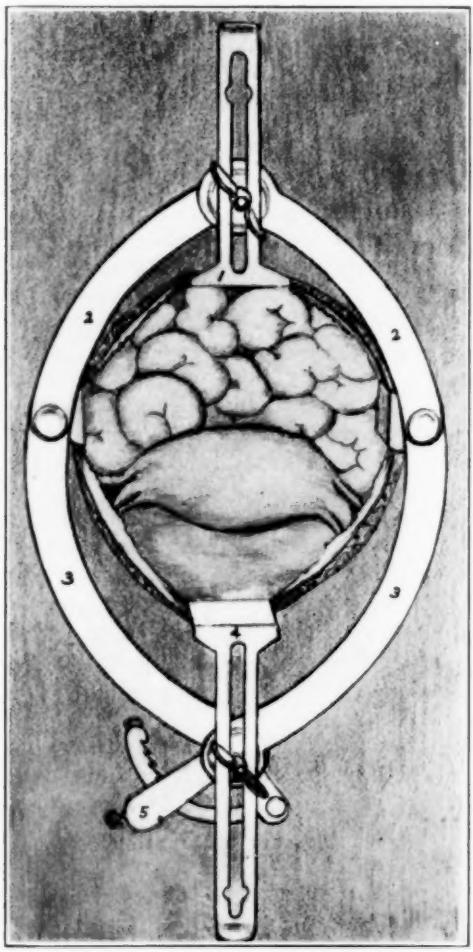

FIG. 5.—Hysterectomy. Both adjustable blades are in place showing adequate exposure obtained before the viscera are excluded by packs. No. 1. Upper angle retractor. No. 2. Upper side arms. No. 3. Lower side arms. No. 4. Lower angle retractor. No. 5. Ratchet catch and set screw.

Rectum, Sigmoid and Colon. The patient is placed on the table with his head slightly depressed from the horizontal and a small pillow under the sacrum. The usual median incision is made and the retractor introduced in such a manner that the long axis is

perpendicular to a line drawn through the anterior-superior spines of the ileum. Packs are then introduced to the rear of the fixed side retractor blades, then the remaining obstructing viscera are excluded by more packs and held out of the way by the adjustable retractors at the angles.

Upper Abdominal Procedures. *Intestinal Resections.* For an intestinal resection the same general setup is employed, with the long axis of the abdominal retractor parallel to the line connecting the superior spines of the iliac crest. The lower angle section, however (Fig. 5, *4*) is on the side away from the surgeon.

Gastroenterostomy. In these procedures the retractor is set with the long axis perpendicular to a line drawn across the abdomen. The end retractors and packs are not placed, however, until the surgical approach to the stomach is completed, *i. e.*, through the mesocolon and gastric omentum. Packs of gauze are then placed at the upper and lower angles and held in place by their respective retractors.

Cholecystostomy and *Cholecystectomy.* This instrument is of greatest value in those fibrotic and densely adherent gall bladders which give the surgeon so much trouble. In these operations the side retractors are set about 2 inches below and parallel to the free border of the ribs. A pack, about 3 inches wide and some 6 inches long, is placed in the upper angle of the wound; the upper angle retractor is then placed in such a manner as to not only retract the abdominal wall but also to hold back the edge of the liver adjacent to the gall bladder. Three or four packs are now distributed in an overlapping manner to exclude the stomach duodenum and small intestine. When these steps have been accomplished and associated a very good exposure of the gall bladder and duct is obtained.

The Retrocecal Appendix. To all surgeons of experiences there comes from time to time the difficult retrocecal appendix. In an obese individual the appendix which is deeply retrocecal and bound down with fibrous adhesions and gangrene presents a very difficult procedure to remove without breaking the appendix and liberating its dangerous contents into the peritoneal cavity. When this retractor is fixed in place it gives good exposure which greatly facilitates the operation.

Conclusions. With this instrument, it is possible to see the field of operation more clearly in abdominal operations. It secures the abdominal wall so that the surgeon may use his assistant during the more difficult phases of the intraäbdominal manipulations. The design of this instrument is simple. It is easily applied and gives positive exposure without slipping.

THE SPECIFIC DYNAMIC ACTION OF FOOD IN ABNORMAL STATES OF NUTRITION.

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In investigations of the metabolic properties of abnormal nutritional states much attention has been given to the possibilities of variations in the specific dynamic action of foods which might characteristically be associated with such states. The reports of many observers[5,25,27,36] suggest that a definite relationship exists between obesity and an abnormality in the specific dynamic action of food. Mason[24] reported that thin states are also associated with an abnormal action. Although Aub and DuBois[3] showed many years ago that the specific dynamic action in persons of unusual shape was normal, Gibbons[16] found a difference between 2 dogs of the same weight but of different shapes. Some investigators[1,15,27] appear to find large variations in specific dynamic action in pathologic conditions which are frequently associated with abnormal nutritional states, whereas essentially normal results have been found by other authors[4,13,26] in analogous nutritional disturbances.

Many of the phenomena associated with the heat effects of foods have been studied in detail. The present knowledge relative to the extra heat production by the various food types is reviewed by Lusk,[23] who draws particular attention to the constancy of this action. With regard to protein, by far the most important food substance in this respect, Rapport and Beard[29] conclude: "That the specific dynamic action of protein is fully accounted for by the summated specific dynamic actions of their constituent amino acids." Rapport[28] has also demonstrated a constant increase of heat production following the ingestion of equal quantities of glycin by different dogs. If these observations be true the development of different heat quantities from the same food by persons who differ only in their food reserves represents an anomalous situation. It seems, therefore, desirable to reëxamine the problem of the abnormalities of specific dynamic action which may be encountered in thin and obese states.

Methods. Three groups of subjects were investigated with reference to the heat effect produced by a fixed meal. Eighteen persons were classified into 5 normal, 5 thin, 8 obese. After variable periods of training in taking basal metabolic determinations the subjects were given a test meal which was eaten in 20 minutes or less. The meal consisted of: Boiled egg, 50 gm.; egg white, 50 gm.; cream, 25 gm.; milk, 200 gm.; sugar, 5 gm.; orange, 70 gm.; bread, 30 gm.; oatmeal, 20 gm.; water, 100 gm.; chicken, 54 gm.; butter, 6 gm.

The total values for this food, as calculated from the tables of Atwater and Bryant[2] are: Protein, 40 gm.; carbohydrate, 52 gm.; fat, 26 gm. The total calories are estimated as 610, with 160 (26 per cent) from protein. The entire meal was eaten by each subject. Metabolism determinations were made before the meal and 1, 2, 3, 4, 6 and 8 hours after the conclusion of the meal. Throughout the test the activities of the patients were restricted. Between tests, for the most part, they sat reading in bed or in a chair. A limited amount of walking around the room was permitted in the interests of comfort. However, before each determination, the customary 20-minute period of relaxation in bed was observed. The heat of metabolism was determined indirectly by the Tissot apparatus. The simultaneous nitrogen output in the urine was not determined and the caloric values were calculated from the uncorrected respiratory quotients.

Observations. Twenty-five determinations were made upon 18 subjects. The essential descriptive data of each subject are summarized in Table 1.

Of the 25 determinations 15 have been considered as having sufficient technical accuracy to warrant analysis. The standards of admissibility which are admittedly rather exacting are: (1) The caloric value for the basal state on the test day must vary by less than 2 calories from the average basal calories of the several determinations performed within 14 days before or after the test; (2) the total heat effect of the meal, as determined from the graphs, must differ from the average value for the particular group by less than four times the average deviation of the mean of the group.[17] Six tests were made upon 5 normal persons. Five of these were satisfactory. Fourteen tests were made upon 8 obese persons and 7 tests on 5 persons were satisfactory. Most of these patients were undergoing reduction of weight according to the dietary principles which have been described elsewhere.[33] Three satisfactory tests were made on 3 of the 5 underweight patients. A summary of the successful and of the unsuccessful determinations appears in Table 2.

The observations of the total calories per hour which were obtained in each group are summarized in Table 3. For the sake of completeness the data on the 10 determinations which were excluded from the averages are given at the bottom of the table.

TABLE 1.—ESSENTIAL DESCRIPTIVE DATA OF SUBJECTS BY GROUPS.

Test.	Date.	Sex.	Age.	Height, inches.	Weight, pounds	Ideal weight, pounds.	Excess weight, per cent.	Surface, sq. m.	Ideal surface, sq. m.	Excess surface, per cent.
					Normal.					
2	Dec. 14, 1928	F	23	64¾	135¾	130	4	1.67	1.64	2
17	May 24, 1929	F	23	64¼	134	130	3	1.65	1.64	1
4	Feb. 1, 1929	M	34	69¼	150¼	160	− 6	1.83	1.89	− 4
20	April 18, 1930	F	21	60½	111½	116	− 4	1.47	1.48	− 1
21	April 19, 1930	F	21	65¼	137	129	6	1.68	1.65	2
					Obese.					
1	Dec. 6, 1928	F	30	60½	145	122	18	1.63	1.52	7
7	Mar. 15, 1929	F	39	62½	344¾	133	159	2.42	1.62	49
24	Aug. 22, 1930	F	40	62½	215¼	133	62	1.99	1.62	23
6*	Feb. 24, 1929	M	37	66¾	146¾					
12**	April 12, 1929	F	39	63½	230	136	69	2.06	1.65	25
14	April 26, 1929	F	39	63½	222	136	63	2.04	1.65	23
25	Sept. 17, 1930	F	25	67¼	201¾	142	42	2.03	1.76	15
					Thin.					
9	April 5, 1929	F	25	67	117	139	−16	1.61	1.73	− 7
11	April 12, 1929	M	24	70½	127¼	158	−20	1.73	1.90	− 9
23	June 6, 1930	F	21	65	109½	129	−15	1.54	1.64	− 6
					Unacceptable.					
5	Feb. 8, 1929	F	39	62½	376½	133	183	2.52	1.62	55
8	Mar. 29, 1929	F	45	64½	239	143	67	2.12	1.71	24
22	April 30, 1930	F	21	63	102	123	−21	1.45	1.57	− 8
15	May 17, 1929	F	39	62½	305½	133	130	2.30	1.62	42
10	April 5, 1929	F	52	65¼	211	148	43	2.03	1.75	16
3	Jan. 20, 1929	F	20	63¾	143	128	12	1.71	1.63	5
13	April 26, 1929	F	39	62½	325	133	144	2.37	1.62	46
16	May 17, 1929	F	39	63½	213	136	57	2.00	1.65	21
18	June 14, 1929	F	31	56	195¾	113	73	1.76	1.39	27
19	Feb. 7, 1930	M	28	66½	109½	145	−25	1.56	1.80	−13

* Amputation. ** Acromegaly.

TABLE 2.—SUMMARY OF ACCEPTABLE AND UNACCEPTABLE TESTS.

Group.	Acceptable tests.	Unacceptable tests.					
		Base line.			Total calories.		
		Too high.	Too low.	Total.	Too high.	Too low.	Total.
Normal	5	...	...	...	...	1	1
Obese	7	2	1	3	2	2	4
Thin	3	2	...	2			
Total	15			5			5

TABLE 3.—TOTAL CALORIES PER HOUR—BASAL AND AFTER TEST MEAL.

Test.	Basal cal.	First hour.		Second hour.		Third hour.		Fourth hour.		Sixth hour.		Eighth hour.	
		Cal.	Inc.	Cal.	Inc.	Cal.	Inc.	Cal.	Inc.	Cal.	Inc.	Cal.	Inc.
						Normal.							
2	57.0	71.9	14.9	68.9	11.9	67.5	10.5	65.1	8.1				
17	54.1	66.0	11.9	65.2	11.1	63.0	8.9	59.7	5.6	56.6	2.5	52.6	−1.5
4	70.4	84.9	14.5	77.8	7.4	78.9	8.5	77.3	6.9	69.0	−1.4	69.2	−1.2
20	51.1	60.2	9.1	59.1	8.0	60.9	9.8	60.3	9.2	57.4	6.3	55.8	4.7
21	58.6	66.5	7.9	65.3	6.7	66.0	7.4	62.9	4.3	62.0	3.4	63.4	4.8
Ave.	58.2	...	11.7	...	9.0	...	9.0	...	6.8	...	2.1	...	1.3
						Obese.							
1	59.9	66.6	6.7	72.1	12.2	69.0	9.1	67.8	7.9				
7	91.2	97.0	5.8	96.0	4.8	95.5	4.3	102.0	10.8	97.5	6.3	87.0	−4.2
24	67.6	77.0	9.4	82.3	14.7	77.8	10.2	73.3	5.7	72.0	4.4	69.0	1.4
6	64.8	77.5	12.7	73.5	8.7	75.0	10.2	71.5	6.7	62.2	−2.6	59.8	−5.0
12	82.5	97.0	14.5	97.2	14.7	95.5	13.0	94.6	12.1	84.6	2.1	85.1	2.6
14	77.7	89.3	11.6	95.9	18.2	91.6	13.9	88.0	10.3	82.1	4.4	94.8*	16.1*
25	56.1	70.0	13.9	68.0	11.9	66.5	10.4	66.5	10.4	62.0	5.9	56.0	−0.1
Ave.	71.4	...	10.7	...	12.2	...	10.2	...	9.1	...	3.4	...	−0.8
						Thin.							
9	60.2	70.8	10.6	76.5	16.3	68.4	8.2	67.9	7.7	67.0	6.8	61.9	1.7
11	60.6	73.9	13.3	68.7	8.1	65.0	4.4	72.9	12.3	64.0	3.4	63.6	3.0
23	47.4	63.8	16.4	61.0	13.6	56.9	9.5	58.5	11.1	54.1	6.7	54.8	7.4
Ave.	56.1	...	13.4	...	12.6	...	7.4	...	10.4	...	5.6	...	4.0
						Unacceptable.							
5	100.0	106.0	6.0	103.5	3.5	107.7	7.7	102.0	2.0	94.0	−6.0	92.1	−7.9
8	70.7	77.9	7.2	81.0	10.3	78.7	8.1	77.1	6.4	75.4	4.7	66.5	−4.2
22	47.2	58.4	11.2	58.3	11.1	55.0	7.8	56.8	9.6	56.5	9.3	54.0	6.8
15	82.2	83.2	1.0	87.0	4.8	80.4	−1.8	83.8	1.6	84.0	1.8	76.0	−6.2
10	67.3	69.3	2.0	69.2	1.9	70.0	2.7	67.6	0.3	68.0	0.7	58.2	−9.1
3	66.5	80.5	14.0	74.6	8.1	68.8	2.3	66.8	0.3	65.0	−1.5	62.0	−4.5
13	76.9	91.0	14.1	91.5	14.6	100.0	23.1	102.0	25.3	90.6	13.7	89.6	12.7
16	66.8	87.0	20.2	81.1	14.3	81.9	15.1	83.4	16.6	77.2	10.4	72.6	5.8
18	48.8	61.2	12.4	61.5	12.7	63.2	14.4	63.9	15.1	58.5	9.7	55.6	6.8
19	51.1	66.3	15.2	68.8	17.7	69.8	18.7	68.1	17.0	56.5	5.4	55.4	4.3

* Omitted.

It may be noted that the average of the basal calories for the normal group, 58.2, is well within the usual range. The obese group has a slightly higher figure, 71.4, as is to be expected.[32] The average for the thin group is 56.1 calories, which is slightly lower than the normal group but not unusual for such patients. The influence of the test meal upon the total calories per hour is summarized in Columns 2 to 13 above. The figures for each hour in each group are averaged separately for purposes of comparison. It may be noted that the maximum caloric increment in the normal group is 11.7 calories above a base line of 58.2 calories per hour. In the obese group the maximum level is 12.2 calories above a base line of 71.4 calories per hour. The thin group has a maximum of 13.4 calories over the base line of 56.1 calories per hour.

It is customary in metabolic work to express observations in terms of "basal metabolic rate." The attention is thereby focussed not

upon the actual heat production, which is truly a rate, but upon the ratio of the observed rate to the rate of an average individual of the same sex, age and surface. This ratio popularly designated "basal metabolic rate" is generally of great practical value. The effect of food ingestion upon this ratio has been calculated and the results are summarized in Table 4. The usual terminology is employed.

TABLE 4.—CHANGES IN BASAL METABOLIC RATE BASED UPON ACTUAL SURFACE.

Test.	Basal metabolic rate, per cent.	Increase over basal metabolic rate.					
		First hour, per cent.	Second hour, per cent.	Third hour, per cent.	Fourth hour, per cent.	Sixth hour, per cent.	Eighth hour, per cent.
			Normal.				
2	− 7.9	24.4	19.4	17.1	13.3		
17	−11.4	19.5	18.2	14.6	9.2	4.1	−2.4
4	− 2.5	18.4	10.0	11.4	9.3	−2.0	−1.8
20	− 6.0	16.7	14.7	18.0	16.9	11.5	8.6
21	− 6.3	12.7	10.7	11.8	6.9	5.6	7.7
Ave.	− 6.8	18.3	14.6	14.6	11.1	4.8	3.0
			Obese.				
1	0.5	11.5	20.9	15.4	13.2		
7	3.0	6.9	5.8	5.2	12.9	7.4	−4.4
24	− 5.7	13.2	20.6	14.3	8.0	6.2	2.0
6*							
12	9.7	19.3	19.6	17.3	16.1	3.1	3.5
14	4.4	15.6	24.4	18.6	13.8	5.9	24.9*
25	−25.2	18.4	15.7	13.7	13.7	8.2	−0.2
Ave.	− 2.2	14.1	17.8	14.1	12.9	6.2	0.2
			Thin.				
9	1.1	14.9	27.3	13.5	13.0	11.3	2.9
11	−11.4	19.6	11.9	6.5	18.1	5.1	4.5
23	−16.8	28.8	23.9	16.7	19.5	11.8	13.0
Ave.	− 9.0	21.1	21.0	12.2	16.9	9.4	6.8

* Omitted.

The average figure for the basal rate for the normal group is −6.8 per cent, with relatively slight individual deviation from the average. The obese group when calculated in the conventional manner averages −2.2 per cent. The sole marked variant being Patient 25. It should be noted that this woman was healthy, young, obese, but in no sense pathologic. The thin group showed an average basal metabolic rate slightly lower than the other two groups, −9 per cent. The influence of the test meal upon the basal metabolic rate and when calculated in the same manner is shown in Columns 3 to 8 of Table 4. The normal group shows an average rise in the first hour of 18 per cent, with a range from 12 to 24 per cent. In the

CHARTS I to III.—Heat effect of test meal.

second and third hours the effect is somewhat lessened with the more rapid drop starting at the fourth hour. At the end of 8 hours the average value was still 3 per cent above the initial level. The figures for the obese group show a somewhat less rapid rise, with a maximum in the second hour and a complete return to normal in 8 hours. In this series, although individual patients (1 and 7) showed relatively less change in the first hour or two, the average peak value, 18 per cent, is as great as that observed in the normal group, although somewhat delayed. The extreme variants in the second hour are 24 and 6 per cent. The thin patients show a percentage rise which is slightly higher than the normals—maximum, 21 per cent. There is a rapid drop at the third hour, with a secondary rise and a failure to return to the base line at the eighth hour by 7 per cent. The individual observations in the first hour vary from 12 to 29 per cent.

Of greater significance than these comparisons of total calories per hour and of metabolic rates, are those of the total heat effects which are made possible by a consideration of the originally noted differences in total calories per hour. The simplest method is to plot the observations of times and caloric increments as ordinates and abscissæ respectively. A smooth curve drawn through these points approximates most reasonably the probable changes in rate of heat production. Consequently, the area beneath the curve represents the total heat production in the observed time interval. The data from Table 3 have been plotted in the following charts, the heavy line in each case representing the composite curve for the group.

The heat production as derived from the areas beneath these curves is summarized in Table 5:

The total heat production for the normal group averages 51 calories in 8 hours. The obese group produced 58 calories in 8 hours and the thin group 67 calories. If only the first four hours are considered the three groups show an even closer agreement, or 37, 42 and 43 calories respectively. The average of all 15 determinations is 57 calories in 8 hours, or 41 calories in 4 hours.

From these data it is possible to calculate the actual percentage increase in heat production, *i. e.*, the number of extra calories produced in 8 hours divided by the number of basal calories for 8 hours, assuming a constant base line. This form of calculation gives an average increase of 11, 10 and 15 per cent in the normal, obese and thin groups respectively. (Column 12, Table 5.)

Discussion. *Types of Subjects.* The patients were classified according to their variations from their probable ideal weights. A variation of less than 15 per cent from the ideal weight was considered within normal limits. Obesity was defined as weight more than 15 per cent in excess of normal. The observed weights ranged from 18 to 160 per cent above the ideal weights. Certain authors[22,27]

CHARTS I TO III.—Heat effect of test meal.

regard the obese state as divisible into groups on the basis of secondary characteristics which are alleged to indicate the etiology of the condition in the given case. Exogenous and hypopituitary types are commonly mentioned. Plaut[27] concludes that, in addition to their less tangible definitive properties, these types may be separated upon the basis of differences in the specific dynamic action to food. Although we are unable to differentiate the several types of the obese state, our group of obese patients showed a

TABLE 5.—EXTRA CALORIES PRODUCED BY TEST MEAL—INTERPOLATED FROM GRAPH.

Test.	Calories produced.						Total calories.	First four hours.	Second four hours.	Basal calories for eight hours.	Increase in basal calories, per cent.
	First hour.	Second hour.	Third hour.	Fourth hour.	Sixth hour.	Eighth hour.					
					Normal.						
2	11	14	11	9	11*	3*	59	45	14	456	13
17	10	12	10	7	8	2	49	39	10	433	11
4	13	11	8	8	5	0	44	40	5	563	8
20	8	9	9	10	16	11	61	36	27	409	15
21	7	7	7	6	8	8	43	27	16	469	9
Ave.	10	11	9	8	8	5	51	37	14	466	11
					Obese.						
1	3	11	11	9	11*	4*	48	34	15	479	10
7	5	6	5	8	18	4	45	24	22	730	6
24	6	13	13	8	10	6	55	40	16	541	10
6	12	10	10	9	4	0	44	41	4	518	8
12	14	15	14	13	14	4	74	56	18	660	11
14	6	17	17	12	14	4*	69	52	18	622	11
25	13	13	11	10	17	6	69	47	23	449	15
Ave.	8	12	12	10	13	4	58	42	17	571	10
					Thin.						
9	6	15	12	8	14	9	63	41	23	482	13
11	12	11	6	8	16	6	59	37	22	485	12
23	16	15	11	10	18	7*	78	52	25	379	20
Ave.	11	14	10	9	16	7	67	43	23	449	15

* From corrected curve.

greatly varied and representative list of secondary characteristics. Both sexes were represented. Young and old individuals were present. A perfect example of the so-called "hypopituitary" type was included as well as a fully developed case of acromegaly who was likewise obese. One subject lacked a leg as a result of an old mid-thigh amputation. Our observations show that, regardless of their varying characteristics, obese persons react in the same manner to a test meal. This opinion is in accord with that of Lauter,[21] who failed to differentiate "exogenous," "hypopituitary" and

"hypothyroid" types on the basis of specific dynamic action to food. The finding of the usual specific dynamic action in a acromegalic is especially noteworthy. The findings of Aub and DuBois[3] of normal metabolic reactions in individuals having artificially diminished surfaces are also supported.

The thin patients were by definition more than 15 per cent below their normal weight, ranging in this series from 15 to 20 per cent. Mason[24] found a definitely increased percentage reaction in thin subjects, and believed this factor to be of importance in the etiology of the condition. Our observations fail to determine a significant deviation from the normal food reaction. Of considerable interest is the fact that Patient 11, who was 24 years of age, had an advanced chronic nephritis. He gave a perfectly normal heat reaction, thereby suggesting that the anomaly of protein metabolism, which is characteristic of nephritis, is not manifest at these earliest stages in protein utilization.

Test Meals. The test meals which have been used by previous workers have been extremely varied. As a rule, since the effect of protein alone was under consideration, high-protein meals consisting of 150 to 200 gm. of lean beef alone, or accompanied by bread, have been used. Some of the earlier investigations have used 400 to 600 gm. of lean beef, and in view of the fact that the object of most of these studies was the determination of the maximum effect producible upon the metabolic rate, such meals were eminently satisfactory. A summary of a few of the test meals which have been used appears in Table 6:

TABLE 6.—TEST MEALS AND DURATION OF TESTS.

Author.	Reference No.	Duration, hours.	Test meal.
Appel and Farr	1	2	200 gm. meat, 1 slice bread and butter.
Aub and DuBois	3	4 to 7	660 gm. scraped beef, small amount of potatoes, kaffee hag.
Aub and Means	4	5	350 to 500 gm. beef cooked with butter, tomato, water.
Benedict and Carpenter	7	3 to 7	200 gm. meat (150 to 360).
DuBois	13	...	10 gm. nitrogen as egg albumen, casein or meat.
Gibbons	16	6	200 gm. meat.
Lauter	21	6½ to 8½	200 gm. beef, 50 gm. bread.
Liebschutz-Plaut, Schadow	22	1	200 gm. meat, 200 gm. bread, 100 gm. fat.
Mason	24	4	200 gm. beef.
Mason	25	4	150 to 200 gm. beef.
Means	26	3	150 to 200 gm. beef.
Plaut	27	3	200 gm. meat, 50 gm. fat, 200 gm. bread, ½ liter coffee, occasionally milk and egg white.
Wang, Strouse, Saunders	36	8	32 to 78 gm. protein as scraped beef, 1 to 2 glasses milk, 2 slices bread, 1 piece butter.

In addition to the great variety of meals employed which prohibits the comparison of their heat effects, many authors record considerable variation in the amount ingested by different subjects in the same series. Wang, Strouse and Saunders,[36] for example, record variations of protein intake between 32 and 66 gm. More important, however, is the fact that average protein ingestion in their obese series was one-third less and in the thin group one-fourth less than in the normal series. Such variations introduce into the analysis the problem of the additive nature of successive increases in protein intake. Benedict and Carpenter,[7] Du Bois[12] and Lusk[23] discuss the experiments of Gigon and others in this connection. Kraus and Rettig[20] question if the specific dynamic action of foods is always strictly additive. As the solution of this problem may still be considered as unsettled, it seems highly desirable to require the ingestion of identical test meals by all subjects.

However, the determination of the total heat effect of a meal presupposes the complete digestion and absorption of the meal in the period of observation. Hawk and his coworkers[18] have shown that the normal period of complete emptying of the stomach for 100 gm. of beef averages 3 hours, with a variation from $2\frac{1}{2}$ hours in the fast types to $3\frac{1}{2}$ hours in the slow. It seems reasonable to suppose, therefore, that many of the test meals which have been used were not completely out of the stomach in the 2- to 4-hour periods of observation. Kraus and Rettig[20] have critically discussed this point, and in their series were able to demonstrate by Roentgen ray examination the complete emptying of the stomach in $4\frac{1}{2}$ hours, using, however, only about 30 gm. of protein. Another factor of importance seems to be the appetizing quality of the meal. Although Hawk[19] has shown that once food is ingested successfully it is probably entirely digested, the importance of the psychic control of digestion, especially with reference to the secretion of proteolytic digestive juices is well established. Such psychic factors might appreciably influence the prompt handling of meals designedly high in protein. Our meal was, therefore, intended to supply the desired protein in an appetizing form and minimize the emotional stress with its own independent heat effect consequent to the forced ingestion of apparently large quantities of unfamiliar foods. At the same time it was important that these foods should leave the stomach promptly, particularly in view of our inability to control complete emptying by Roentgen ray observation. The employment of a mixed meal seemed a requisite for the inclusion of these factors. It may be stated that the components of the meals were weighed on a balance to the nearest 0.1 gm. and that each patient ate the entire quantity in less than 20 minutes. Under these conditions it seems probable that the factors responsible for the extra heat production[23,29] were quantitatively reproduced in each patient.

Base Line. The most vital observation for a successful test is the base line of the curves. This fact becomes obvious when it is recalled that all other determinations are referred to this base. In spite of the obvious importance of the base-line determination few of the recent workers have attempted to insure representative basal caloric values. Some papers mention a single trial basal on the preceding day. Other articles imply no preliminary training. Many of the unusual values which have been reported might perhaps be explained on this basis. Benedict and Carpenter[7] devote many pages to the exhaustive discussion of this point. Attention is called to the normal daily variations in the basal calories. They point out the irrationality of the interpolation of a base line from one day to the next, and after a discussion of the proper basal value to use decide[8] ". . . that the determination of basal values immediately prior to the ingestion of food is the most logical and satisfactory method for studying the small changes in metabolism frequently noted after the ingestion of food." We have adopted this point of view.

Standard metabolic practice requires that a basal determination be performed at least 8 hours after the last meal. High-protein meals require a longer interval before the postabsorptive state is reached. Our series of patients received their basal test 14 to 16 hours after their last meal. In view of the Roentgen ray studies of Kraus and Rettig[20] and of our own heat studies, this period practically insures a true postabsorptive state even for patients who are kept on a "maintenance protein diet" for reduction purposes.

In our experience an adequate training of the patient is essential to securing a correct basal determination on a given test day. Failure in our earliest tests to fully appreciate the importance of this factor is an important cause for their inclusion in our group of unsatisfactory tests. Only one of the three tests made after only one or two preliminary basal determinations was satisfactory. The recent practice has been to perform a series of basal determinations at intervals of 1 to 7 days until the results were approximately uniform. In several of the most recent tests two basal determinations were performed on the subject on the morning of the test in addition to the prolonged training period. The second determination was employed in the calculations, the first being included in the practice period. Again, after the completion of the test one or more basal determinations were made at intervals to check the base line. Many patients who were trained specifically for this purpose of this test had five to seven preliminary tests. The majority were subjects under other investigations and received weekly basals for many weeks.

The first criterion for inclusion of a test in the acceptable group, as described above, permits a variation of the test day basal by 2 calories from the average. Since all of the obese and 1 of the

thin patients were undergoing weight alterations by dietary procedures, with the inseparable alterations in basal metabolic level,[32] the average value used for comparison includes only the determinations made within 14 days before or after the test day. The value of the training period is shown in Table 7, which records the deviation of the basal calories from the average of the recent determinations.

TABLE 7.—DEVIATION OF BASE LINE FROM THE AVERAGE OF TRIAL DETERMINATIONS.

Test.	Number of determinations.	Average calories per hour.	Difference from test day.
	Normal.		
2	3	57.4	0.4
17	1	54.1	0.0
4			
20	4	51.4	0.4
21	5	57.1	0.4
	Obese.		
1	4	59.5	0.4
7	4	90.4	0.8
24	4	66.4	1.2
6	3	63.1	1.7
12	5	82.1	0.4
14	6	78.1	0.4
25	4	55.6	0.5
	Thin.		
9	3	60.9	0.7
11	5	59.9	0.7
23	4	47.1	0.3
	Unacceptable.		
5	3	97.9	2.1
8	4	67.4	3.3
16	3	69.2	2.4
19	6	53.2	2.1
22	4	44.9	2.3
3	2	66.0	0.5
10	2	67.6	0.3
13	3	78.4	1.5
15	4	80.8	1.4
18	4	49.7	1.1

It will be seen from these data that the average deviation of the fifteen acceptable tests is 0.6 calorie and that only two values are greater than 1 calorie. An agreement of this order invites confidence in the reliability of the all-important basal determination and its dependent data.

The depression of the basal level of heat production after a meal has been noted by Lauter[21] and Bernhardt.[11] Benedict and Carpenter[7] state that they have never encountered this phenomenon. Bernhardt discussed this "negative phase" after food, but more especially after work, at considerable length. He emphasized that the negative phase after food was found only in subjects having high basal levels. Two of our normal and 3 of the obese patients

showed this depression. In 1 normal No. 17 and 1 obese No. 25 subject the curve passed below the base line after 7½ hours and the net caloric effect was less than 1 calorie in 8 hours. The curve of the second normal No. 4 cut the base line at 6 hours and flattened out, giving a possible heat effect of 2.5 calories. The curve of No. 6 crossed the base line at 5½ hours and apparently showed a negative heat effect of 8 calories, while No. 7 crossed at 7½ hours with a heat effect of 1 calorie. The 3 patients on whom base-line data are complete No. 6, 7, 25 all showed an elevation of the base line on the day of the test above the average base line. In fact, No. 6, who had the only significant depression, deviated from the average base line by 1.7 calories. It is likewise worthy of note that the total calories under the three significantly depressed curves fall among the lower values of their respective groups.

Of the ten unacceptable curves 5 curves pass below the base line. Of these five curves a demonstrable abnormally high base line was directly responsible for the discarding of two (obese) in spite of the fact that the total heat effect in each case was within acceptable limits. Two other curves, one normal and one obese, which were discarded because the total heat effect was grossly too low, were performed on untrained patients. The fifth curve of this group, which was the fourth specific dynamic action test of a series of five on the same patient (see below), showed two negative phases, at the third hour and again at the seventh hour respectively. Here again a correction of the base line practically nullifies the negative phases. In general, therefore, it may be stated that ten of our twenty-five curves showed some degree of negative phase. Only five were found on technically acceptable determinations. In only two of these was the negative phase greater than 1 calorie, both being associated with high base lines. Only one curve acceptable or unacceptable showed a negative phase when the base line was below the average basal calories, and this was a grossly abnormal curve performed on an untrained subject. Therefore, in accord with Benedict and Carpentet we are unable to demonstrate that the "negative phase" exists as a real phenomenon except insofar as it measures the abnormal elevation of the base line.

The Percentage of Specific Dynamic Action. Throughout medical literature the heat influence of food is expressed in terms of percentage. An attempt to compare the results of different observers shows at once that the meaning to be attached to this percentage factor varies considerably. Certain authors fail to clearly define the ratios employed. Other authors refer to the algebraic difference in percentage of the metabolic rate after food, as compared with the percentage of basal metabolic rate. Mason[25] and Wang, Strouse and Saunders[36] reduce their data for successive periods to terms of calories per square meter per hour and determine the percentage variation of the later values from the basal value. Aub and Means[4]

deal with the total calories per hour and note percentage deviations from the basal total calories. In spite of the variations in point of reference, the percentages so obtained are essentially comparable. In some cases the maximum value obtained is used, in others the value obtained after a definite interval of time. It must be kept in mind, however, that all of these forms of expression deal directly or indirectly with rate of heat production. Such statements to the effect that Patient A has a specific dynamic action of x per cent, therefore, mean that at a certain period of observation the rate of heat production was x per cent above the rate in the basal state. The time factor is entirely ignored. Our data have been arranged to show maximum rate of heat production in this manner and are recorded in Table 4 and Charts I to III. Three features require comment: (1) The time of occurrence; (2) the height of maximum rate; (3) secondary maxima.

The patients of the normal and thin groups show the maximum rate of heat production in the first hour, while the apex of the curves for obese group comes in the second hour. The charts show clearly that, although the composite curves follow these trends, the individual curves of each group show great variety, thus precluding any statement of group specificity. Our data in this respect agree with those of Lauter,[21] Kraus and Rettig[20] and others who found marked individual variation in all groups, but a general tendency for the obese to reach the maximum rate somewhat later than the normal persons. Whether the delay is real or merely due to the small number of patients in each series and to the relatively long time between observations is not apparent.

The numerical value of the maximum rate of heat production varies somewhat with the method of calculation and of expression of results. Our observations when arranged in terms of basal metabolic rate and the differences noted in this ratio following the meal are recorded in Table 4. It will be noted that in the first hour the normal group averages 18 per cent increase, the thin group slightly higher, 21 per cent, and the obese group definitely lower, 14 per cent. These data appear to confirm the observations of Mason,[24] Wang, Strouse and Saunders,[36] Plaut[27] and others, that the obese person has a lower and the thin person has a higher percentage increase in rate after food. However, if the data of the second hour are used, the average of the normals has already fallen to 15 per cent, whereas the obese group has risen to its peak of 18 per cent and the thin group remains at 21 per cent. Moreover, there is a rather marked variation among the individual members of each group—normals, 12 to 24 per cent; obese, 13 to 24 per cent; thin 19 to 29 per cent. When the delayed peak of the obese group is, taken into account the similarity of the ranges of variation of the individuals in each group prevents the identification of a group characteristic, a point strongly emphasized by Lauter.[21]

The percentage change in rate of heat production of our series ranges from 12 to 29 per cent. These results are of the same order of magnitude as those for normal persons as determined by other workers.[22,24,27,36] However, attention must be called to the variations in test meals as used by the various observers. Isolated observations of 50 per cent or more elevation have been noted following meals of excessive protein content.

Two factors exert an important artificial influence upon the numerical values of heat effects when expressed as percentage: (1) The numerical value of the base line, and (2) the variations in body surface. The magnitude of the basal value seriously influences the percentage for a given caloric increment. For example: A 10-calorie increase at a 60 calories per hour base line is equivalent to 16 per cent, but at 90 calories per hour the same increment is only 11 per cent of the base line. If it is recalled that grossly obese persons characteristically metabolize at levels 40 to 50 per cent higher than normal persons and thin persons considerably less, the significance of this fact in the calculation of the percentage specific dynamic action data after the manner of Aub and Means for obese, thin and normal persons becomes apparent. The second factor of importance appears in the calculations which use calories per square meter per hour as a basis. This expression requires the division of the total calories per hour by the body surface. Aub and DuBois[3] pointed out that subjects with smaller surfaces have distinctly higher percentage increase after food. A 10-calorie increment in a person with a surface of 1.67 would introduce a variation of 6 calories in terms of calories per square meter per hour and proportionate change in basal metabolic rate expressed as percentage. If, however, the surface is 2.2, as in many obese patients, the apparent variation is 4.5 calories per square meter per hour. Although the caloric increase is constant, an apparent variation is produced if the data are reduced to the described forms. Here again an identical change in rate of heat production produces an apparent depression of percentage of specific dynamic action in the obese and an apparent elevation in the thin. This factor may be minimized by the calculation of the basal metabolic rate and its changes on the basis of ideal weight and surface. The following table records the date for our obese group in the second hour when calculated according to ideal and actual surface.

The basal metabolic rates calculated on ideal weight are higher than upon actual weight, as has been previously discussed.[32] Of more immediate importance, it will be seen that the average specific dynamic rate is increased 4 per cent. This increase is due solely to the use of the divisor, 1.64, the average ideal surface, instead of 2.03, the average observed surface, in dividing the 12.7-caloric increment. Since the numerical value for the ideal surface, 1.64, is quite comparable to that for the normal group, the percentages

for specific dynamic action thus obtained are more essentially comparable to the figures for the percentage specific dynamic action of normals than are the figures based upon actual surface. Our obese patients showed an average of 21 per cent specific dynamic action in the second hour by this calculation as contrasted with 17 per cent by use of the actual surface. Although in our series neither value differs sufficiently from the normal group to be of significance, the point is made that an important faction of the alleged depressions in specific dynamic action in obesity which have been reported by many authors is due to a mathematical convention rather than to an observation of heat effect.

TABLE 8.—INCREMENT IN METABOLIC RATE CALCULATED ON ACTUAL AND ON IDEAL SURFACES—OBESE GROUP.

Test.	Total calories.			Actual surface.				Ideal surface.			
					Metabolic rate.				Metabolic rate.		
	Basal, cal.	Second hour, cal.	Increase, cal.	Area, sq. m.	Basal, per cent.	Second hour, per cent.	Increase, per cent.	Area, sq. m.	Basal, per cent.	Second hour, per cent.	Increase, per cent.
1	59.9	72.1	12.2	1.63	0.5	21.4	20.9	1.52	7.9	30.0	22.1
7	91.2	96.0	4.8	2.42	3.0	8.8	5.8	1.62	54.2	62.4	8.2
24	67.6	82.3	14.7	1.99	− 5.7	14.9	20.6	1.62	14.3	39.4	24.9
6*											
12	82.5	97.2	14.7	2.06	9.7	29.3	19.6	1.65	37.0	61.4	24.4
14	77.7	95.9	18.2	2.04	4.4	28.8	24.4	1.65	29.0	59.2	30.2
25	56.1	68.0	11.9	2.03	−25.2	−9.5	15.7	1.76	−13.8	4.4	18.2
Ave.	...	...	12.7	2.03	− 2.2	15.6	17.8	1.64	21.4	42.8	21.4

* Omitted.

Many patients show a tendency toward secondary and tertiary rises in the heat production curves. The tendency is more pronounced in the normal and thin subjects than in the obese. Three of the normal and all of the thin patients increased their output in the fourth hour with resultant notching of the composite curves. The possibility of an association between these early secondary rises and the fluctuations in response of the gastrointestinal tract to food exists. With regard to the late secondary and tertiary rises, it is our opinion that the reaction is influenced to a large extent by factors quite apart from the test meal. The curves show that 2 of the 5 normals and all 3 of the thin patients failed to return to the basal level of heat production in 8 hours; in fact, 2 of them showed a definite upward tendency at this time. These elevations, we believe, are due rather to the factors of nervous excitement and fatigue resulting from the prolonged confinement of the test which produce an important independent rise in metabolism rather than a delayed influence of the ingested food.

The preceding discussion of the percentage of specific dynamic

action refers to isolated and to average values for maximum rate of heat production. A more proper perspective of the influence of a meal upon heat production requires an appreciation not only of the intensities of reaction but of the durations of those intensities. Lauter,[21] in his analysis, reports his results in terms of calories per 24 hours. He determines the average caloric output for the period of observation and expresses in percentage the variation from the basal calories. Benedict and Carpenter[7] report results in much the same manner, although they select calories per minute as a working unit. The percentage refers, therefore, to the average increase through the observation period. Obviously, the significance of this numerical value is quite different from that of the figures for maximum rate increase. This expression differs from that of maximum rate in that, whereas the former deals with the form of the curve of heat production, the latter is concerned with the area below that curve.

Our data may be presented in a comparable manner. If we assume a constant 8-hour base line it may be noted that in 8 hours the basal calories of the normal group average 466 calories, the obese, 571, and the thin, 449 calories. Since the increments in the respective groups are 51, 58 and 67 calories respectively, the percentage change becomes 11, 10 and 15 per cent respectively. The individual data are recorded in Table 5, Columns 11 and 12. These numerical values bear quite different interrelationships as contrasted to the numerical differences in maximum rate of heat production noted for the respective groups. In fact, it may be stated that no significant variation is apparent in any group.

The figures above described represent the percentage of increase in heat production in 8 hours which might be attributable to the meal in contrast to the percentage of change of rate of heat production which was discussed previously. The statements take into account the entire heat influence of the meal. They are, however, expressions of the ratio of the total caloric increment to the basal caloric output for the corresponding period. It should be noted that, although this method of expressing percentage of specific dynamic action has much more logic to commend it than the statements of maximum rate observation, it is subject to one of the same criticisms, namely, that the numerical value of the ratio is influenced by the size of the basal value. Benedict and Carpenter[7] point out how the total heat effect forms but an insignificant percentage change if the effect of a single meal upon the total heat production for 24 hours is noted. Our normal group, for example, had an average 24-hour basal heat production of 1400 calories. The 51 calories of the meal increased this value by less than 4 per cent. In our above calculations the basal calories for only the period in which the heat influence was manifest is used, that is, 8 hours, the percentage is accordingly 51 calories in 466, or 11 per

cent. Thus, as in the discussion of maximum rate, it may again be seen that identical heat quantities produce dissimilar percentage values at high and low basal levels.

Quite apart, therefore, from the varieties of meaning which may be attached to the term "percentage of specific dynamic action," it is debatable whether this form of expression affords a proper description of the phenomena involved. The use of the percentage values for maximum rates of heat production and for total heat effect may be of help in apportioning the importance of the many factors which contribute to the total 24-hour heat production of a given individual. On the other hand, however, the magnitude of the all-important basal level is affected by a number of factors, such as age, sex, surface, which are independent of and bear no reciprocal relation to the heat produced by standard test meal. Therefore, for the purposes of the comparison of heat effects of a meal in different individuals . . "The computation of the percentage of the increment is . . . open to serious criticism, and it is difficult to see how such percentages can have real significance." (Benedict and Carpenter.[9])

Total Heat Production. As has been emphasized by Benedict and Carpenter,[7] Lauter,[21] Kraus and Rettig,[20] a true appreciation of the thermal effects of a meal is obtained by focussing the attention upon the total caloric increment which may be observed. Attention must be given not only to the intensity of heat reaction but also to the duration. Given repeated observations of time and intensity, the estimation of the total heat effect is mathematically approximated by the determination of the area beneath a smooth curve drawn through the plotted caloric increments and their respective time factors. The value of such a curve is, of course, dependent upon not only the accuracy of the observations but upon their number. Theoretically, points at 15- to 30-minute intervals are desirable. Practically, 1-hour intervals were feasible. The possibility of the failure of the peak of the production to coincide with an observation time undoubtedly tends to diminish the curve area. However, an appreciable deviation from any observed maximum point would result in a very sharp curve peak which, in consequence, would have only a minimal influence on the total curve area. In spite of the admitted inaccuracies, the area so described gives the best idea of the true effect of the meal on metabolism.

The data which have been detailed above in Table 5 show a heat production of 51 calories and 58 calories for the normal and obese groups respectively. The average deviations of the individual subjects from these means is 7 and 11 in the two groups, or 14 and 19 per cent from the mean. The thin group averages 67 calories with a ±9-calorie deviation, or ±14 per cent from the mean. The entire 15 observations average 57 calories ±17 per cent. In view of the fact that a deviation of but 1 calorie in the base line

determination produces an 8-calorie, or 14 per cent, deviation in the 8-hour curve, it may be assumed that the error in the determination of total heat effect is on the average no greater than that of the Tissot apparatus alone. The apparently large percentage error is due to the small numerical value of the total heat effect rather than to the technique.

An examination of the curves (Charts I to III) shows a considerable individual variation in each of the three groups. In each group curves of the high type of short duration and the low type of longer duration are represented. The factors producing these individual variations in heat production may in part be related to the natural variations in stomach emptying time as well as to the less demonstrable factors in the digestion and absorption cycles. The close resemblance in the three groups of not only the total area but also the contour of the composite curves is very striking. It may be noted that there is no relation whatsoever between the height of the curve peak and the total area, thus emphasizing the fallacy of confusing maximum rate of heat production with the true specific dynamic action of a meal.

Lauter[21] has criticized in detail the experiments of Plaut and similar work, pointing out the inadequacy of tests lasting 4 hours or less. Again, Kraus and Rettig[20] have shown by Roentgen ray that the average complete emptying of the stomach was 4½ hours for their test meal. Although Benedict and Carpenter[7] indicated the possibility of an elevation of the basal level in prolonged experiments, our curves suggest that in the 8-hour period we have employed the latter factor is at a minimum. Our data likewise emphasize the protest of Lauter against the use of short experiments. While undoubtedly the principal effect of a meal is manifest in the first 4 hours, approximately one-third of the total heat production occurs in the second 4-hour period.

An examination of the contours of the curves shows delayed secondary and even tertiary rises. These are more conspicuous in the normal and thin groups. The latent rises, as stated above, are perhaps associated with extraneous factors, such as fatigue, which of themselves produce elevations above the basal calories. Benedict and Carpenter[7] have discussed this point at length. An analysis of the hourly heat production data, as shown in Table 5, indicates that in the first half of the experimental period the heat production in all three groups was very closely comparable. In fact, the average figures for 4 hours are normal group, 37; fat, 42, and thin, 43 calories. The major effects of the meal are to be expected in this period, and it is in this period that the observed heat values are practically identical. Much more variation occurs in the second 4 hours. The group figures are 14, 16 and 23 calories respectively. The bulk of the differences in the various groups falls, therefore, in the period of diminished food influence. These facts

support the conception that in the late hours of our tests extraneous influences produce the largest fraction of the difference between the thin and the other groups.

From the above discussion, it may be concluded that the total heat effect of the test meal does not vary significantly in the different groups of subjects. The observed deviations are small and for the most part explicable as resultants of secondary factors. The individual members of each group show a considerable variation in rate of maximum heat production and in time of occurrence of the maximum rate. However, the total heat production is remarkably constant not only in the three groups but in the entire series.

Thermal Properties of the Meal. The average value for the extra heat produced by this test meal is 57 calories. This figure is admittedly based upon but 15 determinations. Although the demonstration of the absolute value of the heat effect is dependent upon a much larger series, it is of interest to compare this figure with the data of other authors. Lusk[23] and Kraus and Rettig[20] have shown that 30 per cent of the ingested protein calories are given off as extra heat. Our use of a mixed meal precludes our discussion of pure protein effects, nevertheless, it may be observed that 30 per cent of the 160 protein calories of our meal is 48. Our value for the entire meal, 57 calories, is not inconsistent with the figure suggested by Lusk and Kraus and Rettig. Benedict and Carpenter[7] suggest that the extra heat production from an average meal approximates 13 per cent of the protein calories, 8 per cent of the carbohydrate and 2 per cent of the fat, with an average figure of 6 per cent for the "cost of digestion" of a normal mixed meal. These values when applied to our meal of 40 gm. of protein, 52 gm. of carbohydrate, 26 gm. of fat indicate a heat effect of around 42 calories. The total caloric value of the meal is 610 calories. The 57 calories of extra heat production represent a "cost of digestion" of 9 per cent. This value is somewhat higher than the 6 per cent suggested by Benedict and Carpenter,[7] which may perhaps be explained by the relatively high protein content of this meal.

The problem of the source of the extra heat which is developed has been attacked from many angles. Much discussion has centered around whether protein or carbohydrate alone or in combination provide the extra calories. For the most part, evidence is obtained from the observations of respiratory quotient and nitrogen output. No nitrogen observations were made on this series. However, the data relative to respiratory quotients are quite suggestive. The respiratory quotient figures for the normal and obese groups are recorded in Table 9.

The quotients in the normal series do not differ greatly from those of other authors. There is a definite rise in the respiratory quotient during the first 2 hours accompanying the maximum heat production and a subsequent fall to nearly the initial level. Both protein and

carbohydrate appear to contribute to the extra heat production. In the obese group the average value for the second hour, the time of maximum heat production, is slightly higher than the basal. It is of interest that many of the highest values for respiratory quotients coincide with the peaks of the heat production curves. Even No. 7 shows both the highest respiratory quotient and the apex of heat curve to occur together in the fourth hour. However, in view of the general depression of the respiratory quotient, the failure of any of the average values to reach 0.8 and the practical constancy of the average values during the time of maximum heat production (the first 4 hours), it seems justifiable to suggest that, as far as may be judged from the respiratory quotient, the source of the extra heat is not much different from the source of heat in the basal state. It seems possible that the extra heat is supplied in this event not only by protein and carbohydrate, but that a fair percentage is derived from the combustion of fat.

TABLE 9.—RESPIRATORY QUOTIENTS OBSERVED BEFORE AND AFTER TEST MEAL.

Test.	Basal.	First hour.	Second hour.	Third hour.	Fourth hour.	Sixth hour.	Eighth hour.
			Normal.				
2	0.790	0.834	0.760	0.767	0.757		
17	0.825	0.860	0.861	0.839	0.871	0.815	0.811
14	0.780	0.830	0.832	0.828	0.864	0.810	0.820
20	0.848	0.870	0.833	0.825	0.860	0.840	0.839
21	0.770	0.796	0.765	0.762	0.765	0.785	0.808
Ave.	0.783	0.838	0.810	0.804	0.823	0.812	0.819
			Obese.				
1	0.788	0.765	0.802*	0.758	0.713		
7	0.758	0.752	0.738	0.775	0.780*	0.842	0.910
24	0.773	0.756	0.852*	0.768	0.708	0.790	0.823
6	0.698	0.700*	0.689	0.700	0.718	0.678	0.692
12	0.830	0.791	0.807*	0.779	0.773	0.806	0.830
14	0.730	0.723	0.794*	0.780	0.758	0.746	
25	0.720	0.733*	0.721	0.705	0.727	0.706	0.719
Ave.	0.757	0.746	0.772	0.752	0.740	0.761	0.795

* Peak of heat curve.

Unacceptable Determinations. Of the series of 25 tests 10 have been set aside as unacceptable on technical grounds. These tests illustrated practically all of the discoverable and several unexplained errors in the method. Abnormal base-line variations were discussed above. Five tests were discarded because the base line deviated from the average of the trial basal calories by more than 2 calories. Three were obese and 2 were thin. Four of these patients had apparently been adequately trained, but upon the test morning 1 patient (obese) showed a base line far lower than the average and 4 (2 obese and 2 thin) far higher.

Five tests (1 normal, 4 obese) were discarded because of too great a deviation of the estimated total heat production from the mean of the respective group in spite of the fact that the base lines were apparently satisfactory. In any series of observations made under apparently identical conditions, isolated observations are frequently made which differ widely from the rest of the series. The more complex the proceeding under investigation, the greater does the intrinsic potential variability become. Some relatively simple criterion of admissibility of data is desirable and is provided by general practice.[17] If the deviation of an observation from the mean of the series excluding this value is four times the average deviation of the remaining observations from their mean, the figure may legitimately be excluded as of little practical value. The heat production in these cases varied between 7 and 135 calories, with an average deviation of 48 calories. Three of the 5 gave total heat productions of 28, 11 and 7 calories respectively. The first 2 of these were inadequately trained, with a strong probability of an abnormal elevation of the initial base line. One patient was normal in physique, the other 2 obese. The remaining 2, both obese, gave 135 and 95 calories respectively. No explanation is obvious for these phenomena.

A review of the entire 10 discarded curves shows that there is no tendency for these curves to fall in any single group. The division, furthermore, of the obese into the very high and very low groups is about equal. The average calories per hour for these 10 discards is 62 ±39 or ±64 per cent, as compared with 57 ±10 or ±17 per cent, the average of the accepted tests.

The influence of external temperature upon the specific dynamic action of food has been studied by Rubner.[31] Although our investigations were not primarily concerned with this phenomenon, certain pertinent facts may be recorded. The tests were made at intervals over a period of $1\frac{1}{2}$ years. With the Tissot apparatus the room temperature does not indicate the temperature of the air breathed, which comes directly from out of doors. Also bed clothing was utilized to the point of maximum comfort of the patient so that the room temperature does not reflect the skin temperature. Successful determinations were made at room temperatures varying from 18° to 27° C.; average, 23° C. None of the abnormal base-line determinations were associated with unusual room temperatures. Of the abnormally low curves, one was done at 18°, another at 24°, while the high curves were all done above 23°—one on a summer day at 27° C. One low curve and one high curve done on the same patient 2 days apart had the same room temperature.

It may be stated, therefore, that our experiments do not show any significant influence of room temperature on the determination of heat effect of food as it is usually performed and at the range of temperatures normally encountered in hospital practice.

Repetitions of Specific Dynamic Action Test on the Same Person. Specific dynamic action tests were repeated on 3 subjects. Tests 2 and 17 were performed on a normal individual with an interval of 6 months. The first determination unfortunately ran only 4 hours, the last 4 hours being interpolated from a theoretical 8-hour return to base line. The total effect shown on the two curves is 59 and 49 calories respectively, which is as close an agreement as seems possible with the technique.

Three tests, Nos. 12, 14 and 16, were done on the obese patient, who was also an acromegalic, over a period of 5 weeks during which she lost 17 pounds. Two of the tests were technically acceptable, showing 74 and 69 calories respectively, a very satisfactory agreement. The third test was discarded because of a 2.4-calorie deviation of the base line from the average. The calories produced by this patient were the highest found in the obese group. Certain authors report a marked depression in the specific dynamic action of food in the "hypopituitary" type of obesity. It is worthy of emphasis that this patient, who suffered from a well-established pituitary disorder and who was also obese, did not show any evidence of a depressive influence of the pituitary upon the specific dynamic action of food.

Five tests were done on an obese patient over a period of $1\frac{1}{2}$ years, during which time she lost 151 pounds by dietary methods.[33] Test 7, in March, 1929, and Test 24, in August, 1930, were the only acceptable curves. They showed heat effects of 45 and 55 calories respectively. The weight change between these two tests was 129 pounds. Test 5 was performed upon admission, and unfortunately showed an abnormal base line associated with inadequate training. If this base line might be corrected for the deviation from the probable true basal calories the heat-production curve would become practically identical with that of Test 7. An entirely unexplained phenomenon was associated with Tests 13 and 15, which were performed 3 weeks apart after 3 months of training. Although the base-line deviations in the 2 cases were 1.9 and 1.7 respectively, just within the prescribed limits, the total calories observed were 135 and 22 respectively. A careful review of the technique in both instances has failed to supply evidence as to the cause of either of these deviations. The occurrence of a very high and a very low test between two perfectly normal determinations is noteworthy. It is also of importance that the five curves of this patient show a marked dissimilarity in shape. No. 7 showed a typical slow rising markedly two-humped curve, while No. 24 showed a single high peak in the second hour, with subsequent sharp drop. It may likewise be remarked that the maximum percentage rise in basal metabolic rate in No. 7 was 13 per cent in the fourth hour and in No. 24 21 per cent in the second hour, a difference of 8 per cent. The observed increments in calories per hour at these times were

10.8 and 14.7 calories respectively—a difference of but 4 calories. However, the basal calories were 91 calories per hour, with a surface of 2.42 sq. m. in the first instance, and 67 calories per hour, with 1.99 sq. m. of surface in the second. In the calculations of basal metabolic rate these factors produce an artificial magnification of the numerical difference between the increments in total calories per hour. If the ideal surface is used in the calculations in both instances the values for increase in rate of heat production become 18.3 and 24.9 per cent respectively—a difference of 6 per cent.

Considerable emphasis should be placed upon the variety of response to food obtained in this case. Although this patient and the one preceding were both well trained and coöperative, only two acceptable tests were performed in each case. Variations of the type and magnitude described in both the acceptable and unacceptable classes cannot represent the sudden institution of new or characteristic metabolic phenomena. For example, quite opposite conclusions regarding the influence of weight loss upon specific dynamic action would be drawn from the comparison of Test 7 with Tests 13 and 15, and yet Tests 13 and 15 were performed only 3 weeks apart. This experience suggests caution in the making of deductions from isolated observations.

The results of these repetitions of the specific dynamic action test are in accord with those of Lauter,[21] Means[26] and others who found no appreciable difference in heat effect upon repeated tests in the same individual. Our experience also suggests that there is no constancy of curve type which is characteristic of an individual—far less of a group. The influence of change of weight upon the specific dynamic has been reported by Mason,[25] Rolly[30] and others. When properly weighted our observations exhibit no important alteration of the heat effect of food following a small or a large loss of weight.

Benedict and Carpenter[7] indicate that evidence exists that specific dynamic action may vary with nutritional states and, more especially, it is depressed in starvation. The observations reported on the above patient who was maintained for much of 1½ years on the reduction diet which has been described[33] show that here again no evidence of physiological starvation exists in spite of prolonged adherence to diets of 500 to 700 calories.

Specific Dynamic Action as a Factor in the Development and Maintenance of Nutritional States. Among the many factors which have been alleged to be of importance in the development of obesity, a depression of specific dynamic action takes a prominent place.[25,27,36] Not only is it felt that obese persons have a lowered specific dynamic action, but that obese states can be classified into several subgroupings on the basis of variations of reaction.[27] Von Noorden[35] showed that a daily excess consumption of 200 calories would lead in the course of a year to a deposition of 17 pounds of fat, or 20

pounds of fat tissue. Du Bois[12] calculates that an excess of 89 calories per day would add 8 pounds body weight per year. The excessively obese patient probably gains weight at 20 pounds per year or faster, while the milder degrees approach more nearly the lower rate. The caloric excesses, therefore, vary from 90 to 200 calories per day. Benedict and Carpenter[7] state that, on the average in normal people, 6 per cent of a mixed meal is used for its specific dynamic effect. Therefore, on an average caloric intake of 2500 calories per day, 6 per cent, or 150 calories, would approximate the extra specific dynamic heat. The development of obesity within 10 to 15 years on the basis suggested by Du Bois would require a real drop in this 150-calorie factor, certainly to 100 or even 75 calories, or, in other words, a 33 to 50 per cent diminution of total heat effect in the mild cases and a total absence of specific dynamic action in the severe grades. Depressions of these magnitudes should be readily demonstrable.

From the data described and discussed above it will be apparent that we have discovered no significant difference in the heat of reaction to food in either mild or severe grades of obesity as compared with normal persons. We are, therefore, in accord with Lauter,[21] who denies an abnormality in specific dynamic action any rôle whatsoever in the initiation of obese states. Furthermore, our group of obese patients included several of the alleged types of obesity. All were found to react in the same manner. It does not, accordingly, seem possible for us to classify various forms of obesity on the basis of variations of specific dynamic action.

Mason[24] believes that an elevation of the specific dynamic action is in part responsible for consistent thin states. Although our data on this point are less numerous than for the obese state, the observed figures indicate rather clearly that no sufficiently large deviation in extra heat production could be present to account for a caloric loss sufficient to explain this state. If the tendency toward greater fatigability in the undernqurished during a long experiment is considered, our data show that there is no appreciable difference between the normal and the thin group and far less between obese and thin groups.

The data of this series of patients justify the statement that the development of the various nutritional states is not the result of variations in the quantities of extra heat produced by food in these individuals. These data, however, provide no index of the physiologic response of the subject to this extra heat. It may be noted that in normal persons test meals which utilize 40 gm. of protein cause a rise in basal metabolic rate of 20 per cent within an hour after ingestion. Changes in the rate of heat production of such magnitude necessarily produce abrupt alterations in the existing physiologic status. Although the extra heat quantity which is produced by a fixed meal may be identical in the normal, the obese and

the thin, the physiologic readjustments which are necessitated by this increment are not necessarily the same in the three states.

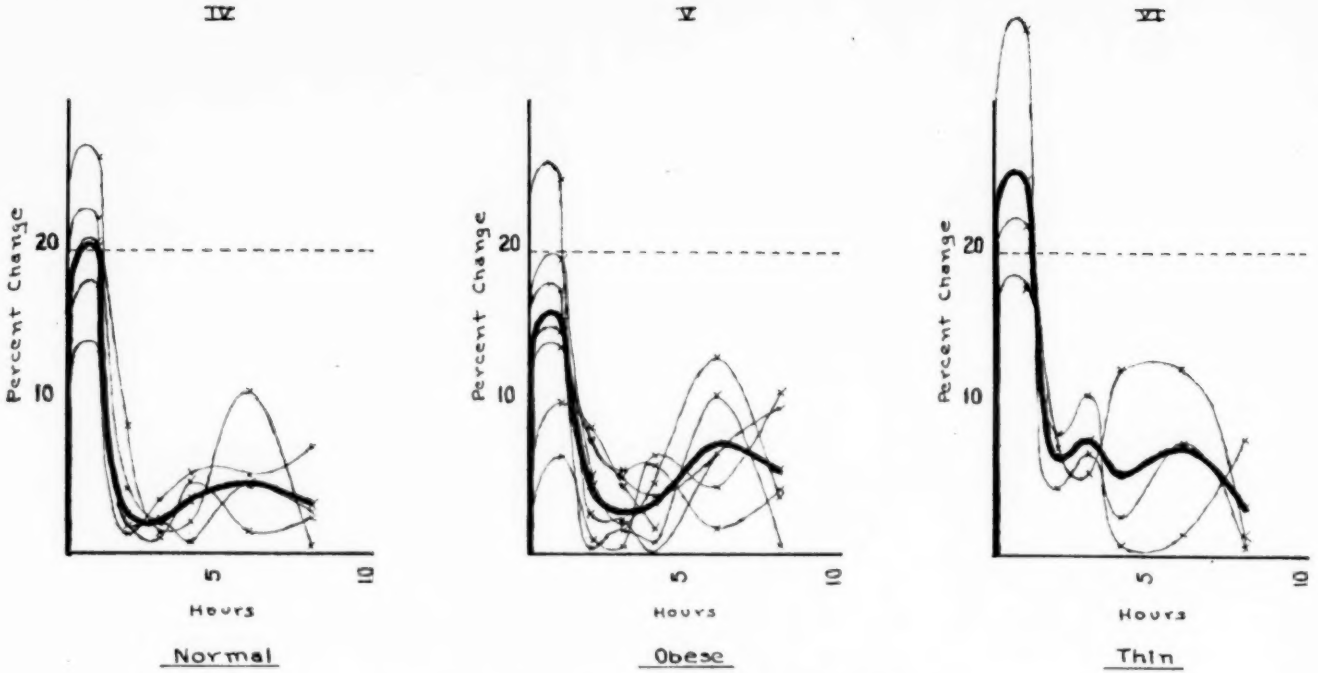
The physiologic load which is thrown upon the organism by this sudden alteration of the heat production is unique. Many intricate and automatic readjustments are necessitated, especially in the departments of circulation and temperature regulation. Since the reserve capacity of the organism as a whole is always more than adequate to care for any possible rate of heat production if the alteration is gradual, it is obvious that observations of maximum rate of heat production afford no measure of the physiologic strain. The load lies in the abruptness with which the body is called upon to readjust to new levels of heat production. It is, therefore, measured not by the maximum rate of total heat production but by the rate at which the existing rate of heat production is altered.

An attempt has been made to obtain a relative numerical measure of the physiologic load which was thrown upon our normal patients by the test meal employed. The basic observations are those of total calories per hour for the successive periods. However, instead of noting the relationship of each observation to the basal determination, the observation is compared with the rate of heat production for the hour immediately preceding. The numerical difference is then divided by the total heat production of the preceding hour in order to give the percentage change, in other words, the rate of change of the rate of heat production. These data have been arranged in Table 9 and plotted in Chart IV.

From the chart it will be seen that immediately following the ingestion of food the curve rises to a sharp peak at the first hour. It is quite probable that the true peak of this curve is obscured by the use of hourly observations rather than those at shorter intervals. For the second and third hours the rate of heat production does not change significantly the low part of these curves corresponding to the nearly flat tops of the curves of rates of heat production (Chart I). The secondary short slow rise with the maximum in the sixth hour represents the period in which the heat effect of the meal is rapidly diminishing and the total metabolism returning to normal. This analysis shows clearly that following a meal the body is required to readjust itself within an hour to a change in heat production of 20 per cent. The subsequent changes are small and comparatively unimportant. The important physiologic strain, therefore, occurs in the latter part of the period of food ingestion and the period immediately succeeding it. Only a small fraction of the total extra heat is produced during this interval, but by the time the maximum rate of heat production has developed, the adaptations to this rate will have been complete. It is, therefore, important to distinguish sharply between the two phenomena which are depicted in Charts I and IV, the rate of extra heat production and the physiologic response to this extra heat respectively.

TABLE 10.—RATE OF CHANGE OF RATE OF HEAT PRODUCTION.

Test.	Basal cal.	First hour.			Second hour.			Third hour.			Fourth hour.			Sixth hour.			Eighth hour.		
		Cal.	Diff.	Per cent.	Cal.	Diff.	Per cent.	Cal.	Diff.	Per cent.	Cal.	Diff.	Per cent.	Cal.	Diff.	Per cent.	Cal.	Diff.	Per cent.
										Normal									
2	57.0	71.9	14.9	26.1	68.9	3.0	4.1	67.5	1.4	2.0	65.1	2.4	3.7						
17	54.1	66.0	11.9	22.0	65.2	0.8	1.2	63.0	2.2	3.4	59.7	3.3	5.2	56.6	3.1	5.1	52.6	4.0	7.0
4	70.4	84.9	14.5	20.5	77.8	7.1	8.3	78.9	1.1	1.3	77.3	1.6	2.0	69.0	8.3	10.8	69.2	0.2	0.3
20	51.1	60.2	9.1	17.8	59.1	1.1	1.8	60.9	1.8	2.1	60.3	0.6	0.9	57.4	2.9	4.8	55.8	1.6	2.8
21	58.6	66.5	7.9	13.5	65.3	1.2	1.8	66.0	0.7	1.0	62.9	3.1	4.7	62.0	0.9	1.4	63.4	1.4	2.2
Ave.	...	...	...	20.1	...	...	2.4	...	...	2.0	...	...	3.3	...	...	5.5	...	...	3.1
										Obese.								
1	59.9	66.6	6.7	10.0	72.1	5.5	8.2	69.0	3.1	4.3	67.8	1.2	1.7						
7	91.2	97.0	5.8	6.3	96.0	1.0	1.0	95.5	0.5	0.5	102.0	6.5	6.5	97.5	4.5	4.4	87.0	10.5	10.7
24	67.6	77.0	9.4	13.9	82.3	5.3	7.5	77.8	4.5	5.5	73.3	4.5	5.9	72.0	1.3	1.7	69.0	3.0	4.1
6	64.8	77.5	12.7	19.6	73.5	4.0	5.1	75.0	1.5	2.0	71.5	3.5	4.7	62.2	9.3	13.0	59.8	2.4	3.9
12	82.5	97.0	14.5	17.5	97.2	0.2	0.2	95.5	1.7	1.7	94.6	0.9	0.9	84.6	10.0	10.5	85.1	0.5	0.6
14	77.7	89.3	11.6	14.9	95.9	6.6	7.4	91.6	4.3	4.3	88.0	3.6	3.9	82.1	5.9	6.7			
25	56.1	70.0	13.9	24.8	68.0	2.0	2.8	66.5	1.5	2.2	66.5	0.0	0.0	62.0	4.5	6.7	56.0	6.0	9.6
Ave.	...	...	...	15.3	...	...	4.6	...	...	2.9	...	...	3.3	...	...	7.1	...	...	5.7
										Thin.								
9	60.2	70.8	10.6	17.6	76.5	5.7	8.0	68.4	8.1	10.6	67.9	0.5	0.7	67.0	0.9	1.3	61.9	5.1	7.6
11	60.6	73.9	13.3	21.9	68.7	5.2	7.0	65.0	3.7	5.3	72.9	7.9	12.1	64.0	8.9	12.2	63.6	0.4	0.6
23	47.4	63.8	16.4	34.6	61.0	2.8	4.3	56.9	4.1	6.7	58.5	1.6	2.6	54.1	4.4	7.4	54.8	0.7	1.2
Ave.	...	...	...	24.7	...	...	6.4	...	...	7.5	...	...	5.1	...	...	7.0	...	...	3.1



CHARTS IV TO VI.—Rate of change of rate of heat production.

If now the physiologic load which is thrown upon the obese and upon the thin by the specific dynamic action of food is approximated in the manner described above rather important variations are revealed. Table 9 and Chart V indicate the rate of change of heat production in the obese group. The general form of the curve is quite comparable to that of the normal group. The significant point is that the maximum of the composite curve falls at 15 per cent, which is 25 per cent less than for the normal group. On the other hand, the thin group as shown in Chart VI reaches its maximum at 25 per cent, which is 25 per cent higher than the normal group. It will thus be seen that although identical meals produce the same total heat of reaction in normal, thin and obese persons, the physiologic load which this extra heat production throws upon the body is approximately one-fourth less in the obese and one-fourth greater in the thin than in the normal. In fact, the thin group bears a 66 per cent greater physiologic strain than the obese in the handling of a meal which is identical in protein, fat and carbohydrate, but particularly in total calories.

The above data bring out the fact that the great difference between the various nutritional states lies, not in the total extra heat production from food, but in the differences in physiologic load which are thrown upon the organism. If it were possible to demonstrate a relationship between this physiologic load and the sensation of satiety which normally determines the limit of food ingestion, an important factor would be exhibited in the chain of causes which determine why fat people unwittingly eat large meals and stay fat and thin people automatically eat small meals and remain thin.

The analysis of a possible relationship between satiety and the physiologic stress resulting from the specific dynamic action of food is difficult and will be reserved for a later discussion. If this relationship may be assumed, it is probable that when the existing rate of heat-production changes at a certain rate, for example, 15 per cent per hour, the body as a whole experiences a feeling of comfort and wellbeing, but when the rate of change is appreciably increased, for example, to 20 per cent per hour, the body rebels against the load and automatically prevents further insult by preventing further food intake—that is, complete satiety. As a corollary of this hypothesis, it follows that when the total metabolism is low a person on general diet will be satisfied by a smaller food intake with its smaller specific dynamic action and total calories than when the total metabolism is high. The normal individual leading a routine existence has a relatively stereotyped curve of variation of heat production throughout the day, with a resultant constant total output. It thus becomes obvious that with the same level of total heat production at corresponding meal times each day a person on a general mixed diet would tend not only to reproduce the same

specific dynamic action with its same resultant physiologic load, but also to repeat the same total caloric intake. It seems reasonable to assume that some such physiologic mechanism is responsible for the well-known fixity of individual eating habits which, in turn, is responsible for the equally astonishing relative fixity of body weight.

From this point of view, the etiology and persistence of abnormal nutritional states becomes more understandable. In the discussion of satiety in normal persons it was assumed that the optimum feeling of wellbeing paralleled a rate of change of heat production of 15 per cent, and that when this rate increased to 20 per cent a feeling of absolute satiety ensued which prevented further food intake. By the application of these same figures to the curves of the thin and obese groups a striking observation will be noted at once. Whereas in the normal persons the satiety point, 20 per cent, corresponds to the peak of the heat curve, in the thin the satiety point was passed long before the peak was reached. This may be interpreted to indicate that the test meal was considerably greater in specific dynamic action and, therefore, in total calories than a meal which these persons would voluntarily have selected. On the other hand, the peak of the obese curve fails to reach the satiety level by 25 per cent, and, in fact, coincides with the level of optimum sensation. A comparable interpretation of this fact would suggest that the test meal, with its fixed total calories and specific dynamic action, would quite fail to satisfy these patients. In other words, if we assume that the test meal, with its 40 gm. of protein and 610 calories, completely satisfied the normal group, the thin patients, if permitted free selection of food, would have been satisfied with much less food, whereas the obese group would require a far greater intake. The selection of the values, 15 and 20 per cent, for the critical points is quite arbitrary, and more careful investigation may reveal entirely different true levels. However, regardless of the levels selected, the fundamental difference between the three groups will persist. Furthermore, it may later be shown that the peaks of the curves of rate of change of heat production fall earlier in the thin group and later in the obese group than in the normal group. If, for example, the peaks were found to be at 20 minutes 40 minutes and 60 minutes in the thin, normal and obese groups the resultant effects upon their relative total food intakes would be accentuations of tendencies described above.

It will, therefore, be seen that the same factors which operate to produce the fixed eating habits and fixed body weights of normal individuals may become perverted in two directions. The resultant extreme in one case is the apparently healthy person who persistently holds a weight 20 to 25 per cent below normal. He functions at a low metabolic level[10] and receives his optimal specific dynamic action stimulus from a small food intake which maintains his weight

by a caloric intake equivalent to his output. The other extreme is the likewise apparently healthy person who maintains a weight 50 to 200 per cent above normal. This person operates at a very high level.[32] He holds his weight, or, as usually happens, slightly increases his weight, because of the correspondingly large caloric intake which is required to produce the requisite rate of change of heat production for optimum sensation. The persistent small intake of the thin and large intake of the obese are probably further aggravated by secondary phenomena both psychic and mechanical. In both of these abnormal states vicious habit cycles are firmly established. It may be emphasized that in neither case does any new pathologic factor in metabolism exist. The thin person stays thin because at his low metabolic level the food intake which produces a specific dynamic action giving him the optimum sensation of comfort amounts to 1500 to 1800 calories. The fat person stays fat because at his high metabolic level a 3000 to 3500 caloric intake is required to give him the same optimum sensation.

If the fundamental abnormality in extreme nutritional states is associated with the metabolic phenomena described above and with the resultant vicious habit cycles, it, therefore, seems possible to correct either of these states by breaking up these vicious cycles. This can be done by dietary procedures. In practice it is a relatively simple matter to take weight from an obese person, but, as a rule, less easy to fatten a thin one. The obvious explanation is that the obese person receives an adequate, though perhaps not optimal specific dynamic action stimulus, three times a day by a maintenance protein diet.[34] This diet is high in protein, with its intense specific dynamic action, but low in both carbohydrate and fat and, therefore, very low in calories. The large caloric deficit thus secured produces rapid weight loss but with comfort. The thin patient, however, presents a much more difficult problem because an alteration in diet produces, not a mere absence of pleasurable sensation as in the obese, but a positive discomfort which frequently amounts to pain and in which the secondary psychic and mechanical factors are also of great significance. The sensations involved in the adherence to a diet 1500 to 2000 calories below maintenance are far less distressing than those which accompany a diet 1500 to 2000 above maintenance. In consequence, persistence and patience are required on the part of the thin person to endure the distress which is caused by the specific dynamic action of a diet containing sufficient additional calories to secure weight gain. A 3500-calorie diet with its total specific dynamic action of approximately 200 calories produces an optimum sense of wellbeing in a fat person but an acute distress in the very thin. In either case, as the weight becomes normal, a reëducation of the sensorium and the establishment of new eating habits is a relatively easy matter.

The suggestion is, therefore, made that specific dynamic action

of food does have an influence upon the development of abnormal nutritional states. This effect is not direct nor is it due to a quantitative difference in the heat of reaction to food. Indirectly, however, the rate of change of heat production which is caused by the heat of reaction to food may be reflected in sensations such as satiety and thus influence the amount and type of food intake which, in turn, are the principal factors productive of weight changes.

Conclusions. 1. The total heat effect of a meal throughout the period of production of this extra heat is the logical basis for comparison of the heat effects of food in different individuals and bears no relation to the maximum rate of heat production.

2. Evidence is described showing that the heat of reaction or "cost of digestion" of a given fixed meal is the same regardless of the state of nutrition of the subject.

3. If the specific dynamic action of food may be related to the development and maintenance of abnormal states of nutrition, it is through the different degrees of satiety produced by the same increase in total heat production which accompany these states and which, in turn may be regulators of both quality and quantity of food intake.

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EXTRA-POLLEN HYPERSENSITIVITY—AN IMPORTANT CONSIDERATION IN THE TREATMENT OF HAY FEVER.

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The treatment of hay fever remains, essentially the same today, as when the principles thereof were first laid down by Blackley[1] in describing and performing the cutaneous test and since their first practical application in England by Noon and Freeman[2] in 1911, and later by Clowes,[3] Koessler[4] and Cooke[5] in this country.

The experience of years has increased our information concerning many phases of the subject. The fundamental problem is that which deals with ways and means of bringing about 100 per cent successful therapeutic results.

As is generally known, the results in hay fever treatment have been poor in the hands of the profession at large, who as a rule make use of the commercial preparations on the market. Many explanations have been offered to account for this. "Because of the limited number of reagents utilized for accurate diagnosis and because of the limited time available for the entailed study of hay fever patients, the indiscriminate use of pollen extracts and employment of shotgun preparations have followed as a matter of course and have been responsible for disappointments."[6]

Yet "even in the hands of men well trained in this specialty, there exists a constant marginal percentage of failures.[7] Hence maxims and rules have been laid down for the purpose of minimizing unsuccessful results. It has been urged to follow strictly the following requisites if one is to obtain the best therapeutic results."[7] (1) Correct diagnosis; (2) Proper treatment by individualization of dosage, or "optimal" dosage. Rackeman[8] believes that success in the treatment demands a course of doses of a size and extent which is optimal for the particular patient; (3) Storage in concentrated form and refrigeration to preserve the potency of the pollen. (4) Pre-seasonal combined with co-seasonal treatment. (5) Avoidance of overtreatment. Does the adherence to the above principles help eradicate the marginal failure? Not so, not even in the best of hands and under closest adherence to the most modern and scientific ideas on the subject as thus far set forth. The question arises, what have we overlooked? May there not be one other factor entirely left out from consideration by most writers, which if properly understood and applied may solve our therapeutic problem? The author is convinced that there exists such a factor.

Many writers had hitherto stated that many seasonal hay fever subjects are also sensitive to substances other than pollen, such as epidermals or foods. They recorded the observation that the offending agents in question tend to make the hay fever worse during the season.

Among the earlier writers on the subject who recognized the necessity of checking up for all types of allergens may be mentioned Eyerman,[9] Balyeat[10] and Kern.[11]

Balyeat made a study of 719 cases of hay fever and found pollen as the sole reactor in only 52.1 per cent.

Kern's discussion on the subject of the "Causes of Failure in Hay Fever Treatment," is very enlightening and proves how some have clearly recognized extra-pollen sensitivity as a major cause in the failure in hay fever treatment. I quote from Kern's article.

"The question might be put, If a hay fever patient is sensitive also to goose feathers why does he have symptoms only in the pollen season? Why do his symptoms not continue throughout the year? The answer is not certain, but this seems a plausible explanation. A patient may be strongly sensitive to ragweed and only very slightly

so to goose feathers. The feather sensitivity is so slight that his mucous membrane in a normal state is not vulnerable but only becomes so when inflamed and therefore more permeable as a result of the more intense pollinosis. Consequently, in the pollen season, the feather sensitivity may succeed in aggravating the disease, and if unrecognized, bring about the failure in pollen treatment." Moreover, recently workers in this field have begun to show renewed interest in these extra-pollen irritants. Thus Rowe[12] concludes in a recent article: "The allergist must study the patient complaining of seasonal hay fever from the point of view of sensitization to other than pollen allergens."

Fosket[13] mentions the importance of checking up for reactions to substances other than pollen in cases in which the routine pollen treatment proves unsatisfactory. Cohen and Rudolph[14] summarize the subject matter clearly and concisely by stating:

"Sometimes there is a coexisting sensitivity to some substances other than pollen which may exacerbate the symptoms during the hay fever season. Further consideration of this point led us to the belief that failure to discover and eliminate these extra factors has been responsible for the majority of failures to obtain relief by specific methods."

In 1929 I wrote: "In a number of cases carefully chosen, showing not any or partial relief, a study of extra-pollen sensitivity was undertaken for the purpose of determining whether or not that might be taken to account for the nonresponse to the treatment. For comparative purposes, the results of such sensitization tests in a parallel series of patients who obtained excellent results from the pollen treatment are also tabulated. The results seem to warrant the conclusion that extra-pollen hypersensitivity may be given as a factor which when present to a marked degree precludes the possibility for complete and successful desensitization in seasonal hay fever treatment." It is my purpose to show herein from the case reports that follow that extra-pollen hypersensitivity is a most important consideration in the treatment of hay fever.

Case Reports. CASE I.—S. H. S., female, aged forty-two years, has been having hay fever for the last eighteen years. She was found sensitive to the ragweed pollens and to plantain. She has been receiving treatments for the past two seasons.

She is intelligent and very coöperative and is greatly interested in her own problem, and shows marked aptitude in understanding all of the complications that surround her malady. She was tested routinely for the pollens as well as for a great number of the inhalant and food proteins by the intradermal method. She was given a list of instructions as to what contacts to avoid and what not to eat.

The very interesting observation had been made by herself, that the slightest contact with dust during the hay fever season immediately predisposed her to the severest seizure of hay fever symptoms. She is careful to avoid that particular offending agent. I made it a point to give her inoculations of dust extract in ascending dosage along with her pollen

treatments and as part of the therapeutic measure during the hay fever season. She appeared very happy one day in September, 1930, when she gladly advanced the information that she was greatly relieved to know that her agonies of eighteen years' duration had finally ended. Strict avoidance of dust and daily injections of small quantities of dust extract (up to 0.3 cc.), then a gradual increase in dosage, and given twice a week, brought about subsidence of symptoms.

She consented to volunteer herself for the purpose of determining whether or not contact at will with particular inhalant proteins, or ingestion of certain food proteins, can actually bring on spells of hay fever symptoms. Since she showed a sensitivity of 5+ to corn, it was decided to allow her to eat her favorite dish once at supper. Symptoms developed, which lasted throughout the night and the following day.

As long as this patient was receiving dust extract inoculations at regular intervals during the hay fever season along with her pollen extract treatments she was in excellent condition. Just as soon, however, as the dust extract was at one time or another left out of her treatment menu she would be seized by hay fever symptoms.

CASE II.—N. K., aged thirty-five years, a janitor in a church by occupation, has had hay fever for the past six years. Up to this year, and for the last three years, he has been receiving treatments regularly pre-seasonally and co-seasonally. The results from the treatment, however, had been persistently poor. This time, in 1930, it was determined, for the first time, that he was sensitive to many inhalants and a few food substances, in addition to the ragweed pollens. He was cautioned against these offending agents. One of the principal reactors was stock dust, and skin reaction to the intradermal test was repeatedly 4+.

He received a thorough course of pre-seasonal treatment which I was planning to continue during the season. Nevertheless, as the late hay fever season set in the results were disappointing.

I was greatly puzzled to find that even on Sundays he would react miserably with marked hay fever symptoms. I reasoned that it could not be the dust he was in contact with, in spite of the precautions which he assured me he was taking. The inoculation of dust extract given him should have protected him. The fact, too, that Sundays brought no relief, excluded dust from consideration as an extra factor. I could not, moreover, understand why his report always included Saturday as a day when he was absolutely free from hay fever symptoms. Finally, it was discovered that the patient was a Seventh Day Adventist, and therefore rested at home, away from his usual occupation, on the Sabbath, or Saturday. It was arranged that he obtain a four-week change of occupation; his symptoms cleared up.

CASE III.—Miss M. H., aged thirty-five years, has been suffering from late hay fever for two seasons. She was under my care last year, with good results. She was found sensitive to many fo od substances. The two principal reactors were beef, 4+, and pork, 5+. On Columbus day, 1930, she invited guests for breakfast. She fried bacon and partook of it liberally. She was soon seized with severe hay fever symptoms.

CASE IV.—H. R., aged thirty-eight years, a physician, was found sensitive to the tree pollens. His principal reaction was to red oak. Proper treatment definitely controlled his hay fever symptoms. He is emphatic in his statement that just as soon as he eats no more than one cherry during the tree hay fever season he is immediately seized by most violent hay fever; he is otherwise free from symptoms.

(The above case was called to my attention by Dr. M. M. Peshkin, of New York.)

Comment. Many other case reports could be cited to illustrate the presence of extra-pollen factors as irritants during the hay fever season, to the extent that they tend to make the hay fever worse and are responsible for the failure in treatment. Only outstanding reports are given here in order not to burden the reader with uninteresting material. Although the most common inhalant substances found to complicate the sensitivity of many of our patients were dust, orris and animal epithelia, yet our case records include the presence of sensitivity to representatives of each group of the inhalant and food series to an equal and as marked a degree.

I found particularly that with the inhalant allergens, it was not sufficient simply to eliminate contact but also to institute actual treatment against such agents as dust or orris, both pre-seasonally and co-seasonally.

With the food substances as complicating factors, elimination of contact or avoidance of ingestion of the particular irritant factor was sufficient to help toward successful results in the hay fever treatment.

Summary. 1. Our knowledge and information concerning the treatment of hay fever has in recent years increased greatly indeed. The outstanding problems have always been directed toward bringing about absolute therapeutic results.

2. The results in hay fever treatment in the hands of the profession at large are generally markedly disappointing. Reasons are cited to explain this.

3. Even in the hands of men well trained in the treatment of hay fever, there exists a marginal percentage of failure.

4. Extra-pollen hypersensitivity may be the cause of such a marginal percentage of failure.

5. In the present study, case reports are presented that tend to show that extra-pollen hypersensitivity is a most important consideration in the treatment of hay fever.

6. Desensitization was found necessary both pre-seasonally and co-seasonally against the inhalant allergens. With foods as complicating factors, avoidance of ingestion during the season was found sufficient.

Conclusion. Extra-pollen hypersensitivity should receive serious consideration when treating patients for seasonal hay fever. All such patients should be tested routinely with the inhalant and food allergens. When found sensitive to the inhalant proteins they should receive desensitization both pre-seasonally and co-seasonally. When found sensitive to foods, these should be eliminated from their diet during the season.

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APPENDICITIS IN CHILDREN.

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The problem of appendicitis in infants and young children is quite different from that in adults. In the first place, especially in infants, a satisfactory history is often difficult to obtain. Parents are prone to overemphasize unimportant events and will very often fail to recall the more important features of an illness. Second, physical examinations on the very young are difficult to do and the findings hard to interpret. The child is sick and often very irritable; besides he is often away from home among strangers and frightened. An infinite amount of patience and time is required before coöperation can be obtained. Differentiation between voluntary and involuntary muscle spasm is often impossible, localization of the maximum point of tenderness is difficult, rectal examination is often unsatisfactory or impossible, and, finally, chest pathology may be hard to rule out. Because of these factors children more than adults consult a doctor late in the disease. Even with the best of coöperation the physician may have a difficult time differentiating the trouble from acute pyelitis, upper respiratory infections, pneumonia, urinary calculi and the ordinary gastrointestinal upsets.

On the other hand, occasionally a diagnosis of acute appendicitis is made in very young infants when the actual condition is a primary peritonitis.

The following report is based on the records of 111 consecutive appendectomies performed on children at the University Hospital, from January, 1920, to January, 1929. All of the children were under 13 years of age. During this same period of time there were in all 700 primary appendectomies performed. Children under 13 years made up 15.8 per cent of all these cases; only 2.6 per cent of these were in children under 5 years of age. Table 1 shows the proportion of children to adults by various authors for different age groups:

TABLE 1.—DISTRIBUTION OF CASES ACCORDING TO AGE.

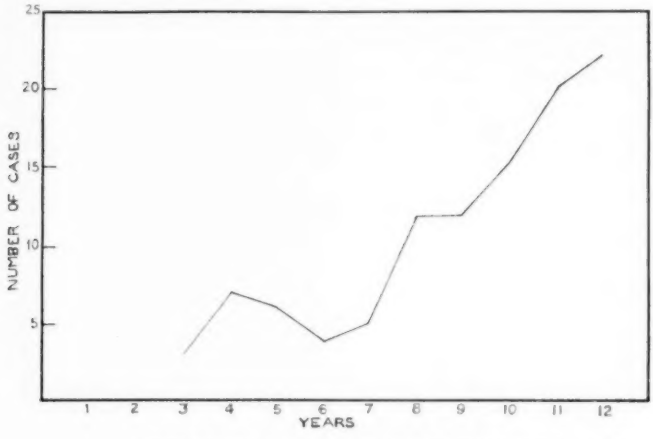
Author.	Number of cases.	Maximum age.	Per cent.
McCosh[1]	1000	15	8.50
McCosh	1000	5	1.70
McCosh	1000	3	0.40
Bellington[2]	742	15	22.00
Hoffmann[3]	2560	4	0.82
Riedel[4]	1222	15	6.70
Fowler[5]	..	..	16.40
Churchman[6]	1223	5	0.73
Churchman	1223	15	16.00
Eliason[7]	..	10	9.40
Eliason	..	5	2.70

Age. The youngest patient was a girl, aged 2 years and 7 months. The next youngest was a boy aged 2 years and 10 months. Both had acute suppurative appendicitis and 1 was complicated by a diffuse peritonitis. Both recovered. Appendicitis in the very young is relatively uncommon. The youngest reported case is that of Corcoran,[8] who reviewed an autopsy on a child 2 days old, in which he found the appendix perforated and believed that this had occurred during prenatal life. Jackson[9] reported another autopsy on a child 40 hours old, who died of mercurial poisoning, whose appendix showed signs of congestion with firm adhesions, binding it down to the neighboring organs. Dixon[10] also reported a case in a premature child 24 days old. Kermisson[11] had a case 11 months old and was able to find records on only 11 other cases near this same age. Abt[12] collected 80 cases under 2 years of age, with a mortality of 50 per cent.

Sixteen per cent of the children in this series were under 5 years of age. Beth reported 20 per cent. Fig. 1 demonstrates the marked increase in the number of cases with each year of life after 7 years; from the age of 2 to 7 years the cases seem to be distributed at a low and almost even rate.

Sex. According to the table of collected cases, most authors have found a predominance of male cases over female. Our figures show almost equal distribution, with 54 per cent females and 46

per cent males. There is no adequate reason why in children one sex should be represented by more cases than the other. In adults, as in children, there was a slight increase in the number of females in the interval and subacute cases, while in the acute cases there was a preponderance of males.



APPENDICITIS IN CHILDREN—ACCORDING TO AGE

FIGURE I.

TABLE 2.—DISTRIBUTION OF APPENDICITIS IN CHILDREN ACCORDING TO SEX.

Author.	Date.	Cases.	Age limit.	Males, per cent.	Females, per cent.
Erdmann[14]	1907	60	..	59	41
Beth[13]	1908	100	12	52	48
Deaver, H. C.[15]	1910	500	15	63	37
Fowler[5]	1912	183	12	63	37
Porter[16]	1918	100	15	48	52
Alexander[17]	1920	500	15	57	43
Beckman[18]	1924	145	..	63	37
Edberg[19]	1926	754	15	52	48
Seeger[20]	1926	61	..	67	33
Farr[21]	1928	889	..	50	50
Peterson[22]	1929	100	6	71	29
Holt[23]	..	101	..	72	28
Richter[24]	..	185	..	60	40
Total		3678		60	40

Seasonal Incidence. The highest number of cases occurred during the fall, with summer ranking second. Alexander[17] found the incidence in children highest in the summer time. There was also noted a definite tendency for the cases to appear in epidemic form.

Infections. Whether or not acute respiratory infections, contagious diseases and gastrointestinal disorders precipitate attacks of acute appendicitis is difficult to prove. Thirteen per cent of

our cases gave a definite history of some recent previous acute infection. Especially prominent were the upper respiratory diseases. There was also 1 case each of measles, whooping cough and scarlet fever. Porter[16] reports as high as 60 per cent previous sore throats and tonsillitis; Richter,[24] 4.06 per cent acute infections, with the presence of some sort of focal infection in 24.4 per cent. Brennemann[22] reports 17 per cent sore throats in 35 cases in hospital practice, while in 10 private cases 9 had an accompanying pharyngitis or tonsillitis. Reiche[26] found 19 cases of acute appendicitis among 7015 cases of diphtheria.

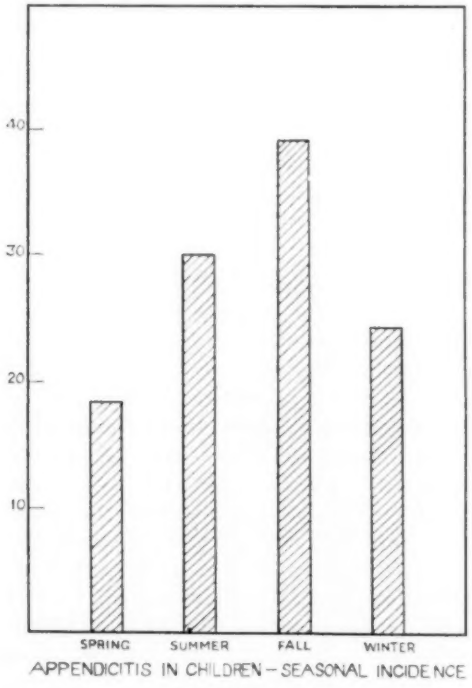


FIGURE II

It must be continually borne in mind that cases with tonsillitis can give symptoms very suggestive of appendiceal infection. Pneumonia, especially of the right lower lobe, is very often mistaken for appendicitis. Several cases were admitted to the hospital with the latter diagnosis which was ruled out only by careful history taking and by thorough chest and abdominal examinations. Roentgen ray examination in such patients may be very helpful. Patients with pneumonia usually appear sicker than those with appendicitis and often have flushed cheeks, dilating alæ and rapid shallow respirations. The temperature, pulse and leukocyte count are

generally higher in pneumonia also. Berger[27] found that in 145 cases of pneumonia in children, seen at the Boston City Hospital, from the age of 2 to 15 years, 25, or 17 per cent, were originally admitted with the diagnosis of acute appendicitis.

Previous Attacks. There was a definite history of previous attacks in 35, or 31 per cent, of our cases. This is higher than any report listed in the table below, probably because of the fairly large number of interval cases seen at the University Hospital.

TABLE 3.—PERCENTAGE OF PREVIOUS ATTACKS.

Author.	Age limit.	Cases.	Per cent.
Helmholz[28]	5	15	6
Helmholz	15	53	30
Mitchell[29]	12	40	6
Fowler[5]	12	183	11
Richter[24]	12	172	22
Gray[30]	12	200	5
Bolling[31]	15	123	12

Classification of Cases. The most satisfactory grouping of cases was found to be the surgicopathologic. The cases were divided into the following groups:

1. Interval appendicitis.
2. Acute suppurative appendicitis.
3. Acute suppurative appendicitis with local peritonitis.
4. Acute suppurative appendicitis with abscess.
5. Acute suppurative appendicitis with diffuse peritonitis.

Each type will be discussed separately and will include clinical and microscopic findings. Each case was classified clinically under one of the following headings: (1) Mild, (2) moderate, (3) severe and (4) moribund.

Every appendix removed was examined both grossly and microscopically by the hospital pathologist and classified under one of the following three headings: (1) Acute recurrent appendicitis (evidence of previous infection manifested by scarring or with the presence of perivascular round-cell infiltration in the serosa); (2) acute suppurative appendicitis; (3) no evidence of inflammation.

1. *Interval Appendicitis.* There were 29 cases in this group. In nearly every record there was a history of one or more previous attacks of rightsided pain accompanied by anorexia, nausea or vomiting. A few cases were doubtful and might possibly be classed as chronic appendicitis. They were explored after thorough study had been made and every other diagnostic possibility had been ruled out. There were also included some cases of subacute appendicitis and some of subsiding acute appendicitis. There were no deaths in this group. Clinically all of the cases appeared mild. Microscopic examination revealed acute recurrent appendicitis in 9 cases, suppuration in 2 and no inflammation in 18. The average leukocyte count was 10,000 and the average polymorphonuclear percentage was 69. The majority of these patients had normal

temperatures, with only 5 over 101° F. The pulse corresponded closely to the temperature.

2. *Acute Suppurative Appendicitis.* This group included 13 cases and was made up of those that showed only suppuration of the appendix with no secondary involvement elsewhere. There were no deaths in this group. Clinically, 3 cases were considered mild, 8 moderately severe and 2 severe. Microscopically, 10 appendices showed supuration; in 3 there was only slight evidence of inflammation. The average leukocyte count was 13,000, with an average polymorphonuclear percentage of 84. In two-thirds of the cases the temperature was normal. In no case was it over 103° F. The pulse rate corresponded fairly accurately with the temperature.

3. *Acute Suppurative Appendicitis with Local Peritonitis.* There were 25 cases in this group, with 1 death. The average leukocyte count was 17,000, with an average polymorphonuclear count of 83 per cent. Seventeen cases were considered moderate in severity and 7 severe. Only 1 was considered mild. All of the appendices showed suppuration microscopically. Eleven cases had an elevation in temperature of 101° to 102° F., but no higher. The pulse rate ran parallel to the temperature.

4. *Acute Suppurative Appendicitis with Abscess Formation.* This group included 33 cases, the largest number for any single class. Besides the abscesses localized around the appendix, there were included those more remotely situated, such as the pelvic, subdiaphragmatic, subhepatic and those in the flank. There were 3 deaths in this group. The average white blood count was 21,000, with an average polymorphonuclear count of 88 per cent. Only 1 case presented mild symptoms, 12 were considered moderately severe, 17 severe and 3 were classed as very severe or moribund. All specimens removed showed evidence of suppuration microscopically. In 1 case the abscess was drained, leaving the appendix in for later removal. Thirteen patients had temperatures of 100° F. or less, while 9 had a fever of 102° to 103° F. The pulse rate was higher in more cases than was the temperature, especially in the more seriously sick children.

5. *Acute Suppurative Appendicitis with Diffuse Peritonitis.* Fortunately there were only 11 cases in this group, as it has the highest mortality rate—3 deaths, or 28 per cent. All of the cases had diffuse peritonitis of appendicular origin. All were considered as seriously sick children on admission. All of the appendices removed showed suppuration. The average leukocyte count was 21,000, with 81 per cent polymorphonuclears. The temperature in all was 100° F. or more; 5 were 103° F. or over. The pulse rates were elevated, but in only 2 cases was it markedly increased. Operation was performed in each case, the appendix removed and the abdomen adequately drained with numerous soft rubber tissue drains of the Penrose type.

Urine Examination. Nineteen per cent of the cases showed abnormal urinary findings. None of these were operated upon until urinary disease had been satisfactorily ruled out.

TABLE 4.—URINE EXAMINATIONS.

Type of appendicitis.	Negative.	White blood cells.	Red blood cells.	Both.
Interval	27	2	0	0
Acute suppurative	10	1	1	1
With local peritonitis	18	7	0	0
With abscess	27	6	0	0
With diffuse peritonitis	8	3	0	0

The highest proportion of abnormal urinary findings was in the group with local and diffuse peritonitis and with abscess formation, probably the result of the toxic effect on the kidneys or due to an inflammation of the right ureter because of inflammation or infection adjacent to it. Helmholz[28] reported 8 per cent with urinary symptoms, while Richter[24] found 6 per cent with abnormal urines.

Leukocyte Count. The highest counts were found in the cases with abscess formation and with diffuse peritonitis. A leukopenia means a very poor prognosis. The only 2 cases with counts below 5000 died; 1 was 3600 and the other 4950.

The time interval between onset of symptoms and time of operation is a most important factor in forecasting surgical pathology and the ultimate prognosis. In the cases where the disease was localized to the appendix or to the neighboring peritoneum the average time interval was 53 hours; while in the cases with abscess formation and diffuse peritonitis the number of hours was increased to 78.

Nearly every case of acute appendicitis should be operated upon as soon as the diagnosis is made, the exceptions being those cases in which a definite diagnosis of diffuse peritonitis can be made, and also in those where the general condition is so bad that operation would surely prove fatal. In these almost hopeless cases supportive and expectant treatment often allows one to perform appendectomy or drainage later, after the disease has localized itself.

Ethylene and ether usually were the anesthetic agents employed. Complete relaxation of the abdominal walls allows the best exposure, least trauma and least contamination. Right rectus incision was employed 78 times, Battle incision 18 and McBurney 15 times.* The abdomen was drained in 54 out of 82 acute cases. Ileostomy was done on 1 patient, with a fatal outcome.

The postoperative complications were: Bronchopneumonia, 2; evisceration, 2; fecal fistulæ, 1; wound infection (severe), 2; chickenpox, 1.

The mortality percentage for the entire group of 111 cases was

* At present the McBurney incision is used in the majority of instances.

6.3. In the interval group it was 0 per cent, while in the acute group, numbering 82 cases, it was 8.4 per cent. The mortality rate for cases over 12 years of age with acute appendicitis of all varieties was 6 per cent. The ages of the 7 patients that died were 4, 5, 9 years and 4 of 11 years. Of the 7 deaths 5 occurred in males.

TABLE 5.—OPERATIVE MORTALITY RATE FOR APPENDECTOMIES IN CHILDREN.

Author.	Year.	Number of cases.	Maximum age.	Mortality, per cent.
Erdmann[14]	1907	100	15	7.0
Riedel[4]	1907	310	10	16.4
Beth[13]	1908	100	12	21.0
Bar[32]	1908	49	10	12.0
Churchman[6]	1909	9	5	22.0
Braman[33]	1909	117	15	17.9
McWilliams[34]	1910	55	10	10.0
		16	5	18.7
Dowd[35]	1910	181	15	6.0
Deaver[15]	1910	500	15	4.6
Mitchell[29]	1912	40	13	25.0
Bellington[2]	1912	115	15	17.8
Fowler[5]	1912	183	12	3.0
Hoffmann[3]	1912	...	10	15.3
Gray[30]	1914	200	12	10.0
Clofton[36]	1915	...	..	4.0
Morf[37]	1917	150	15	8.0
Abt[12]	1917	80	2	50.0
Alexander[17]	1920	500	15	3.0
Helmholz[28]	1924	15	5	47.0
		53	15	5.5
Beekman[18]	1924	145	13	7.5
Bolling[31]	1924	123	15	8.1
Muller[38]	1924	58	15	6.8
Edberg[19]	1926	754	15	5.0
Seeger[20]	1926	61	13	8.2
Farr[21]	1928	889	15	5.9
Peterson[22]	1929	100	6	6.0
Richter[24]	..	208	13	7.2

From the above table one can readily see that the mortality rate is much higher in the lowest age groups.

Postmortem examination was done on 6 out of the 7 patients that died. The cause of death was reported as follows:

1. Embolic pneumonia.
2. Diffuse peritonitis—subdiaphragmatic abscess.
3. Diffuse peritonitis—bronchopneumonia.
4. Diffuse peritonitis.
5. Diffuse peritonitis—ileus, bronchopneumonia.
6. Diffuse peritonitis—ileus.
7. Diffuse peritonitis—ileus.

Conclusions. 1. Acute appendicitis is seldom seen before 3 years of age, but then occurs with increasing frequency and especially after 7 years.

2. Appendicitis in children occurs slightly more often in males than in females.

3. The peak seasonal incidence is in the fall.

4. There was a history of recent previous infection elsewhere in the body in 13 per cent of the cases.

5. There was a history of one or more previous attacks in 31 per cent of the cases.

6. There is a fair degree of direct correlation between the clinical picture and the surgical and pathologic findings. Unfortunately, however, the degree of correlation occasionally is poor.

7. A leukopenia in acute appendicitis usually means a fatal outcome.

8. Nineteen per cent of the cases showed abnormal urinary findings.

9. The most frequent cause of death was diffuse peritonitis.

10. The time interval between onset of symptoms and time of operation is probably the most important factor in determining pathology and prognosis; consequently, early diagnosis followed by immediate appendectomy offers the best hope for a low mortality rate.

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A UNIQUE ANOMALY OF THE BILIARY TRACT. COMMUNICATIONS BETWEEN CYSTIC AND HEPATIC DUCTS WITH OCCLUSION OF COMMON DUCT AND SEPARATE ENTRANCES INTO THE DUODENUM.*

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In studying the gall bladder and biliary tract in a series of necropsies on infants a unique anomaly of the bile ducts was found. It seems sufficiently interesting to warrant adding it to those already recorded in the literature. Any such anomaly, of course, is of practical interest to the surgeon.

The anomalies of the bile ducts and gall bladder are varied and numerous in man as well as in certain domestic animals that have been studied, namely: the cat, dog, sheep, calf and pig. Some of these abnormalities have been described by Gessner,[1] Kehr,[2] Schachner,[3] Eisendrath,[4] Morley,[5] Graham,[6] and Boyden.[7] Various types have been described by these writers but none seem to conform exactly to the anomaly found in the case reported below. Flint[8] mentioned the fact that separate entrance of the common hepatic and cystic ducts into the duodenum occurs but gave no authority for this statement.

Case Report. L. D., a white female child, aged six weeks, was admitted to the University of Virginia Hospital on July 29, 1930. When she was one week old blood was noticed in the stool, followed two days later by seepage of blood from the umbilical stump, vagina, mouth and eyes. There had been no vomiting and jaundice had not been observed. She was born by a normal delivery at term, had none of the childhood diseases and was breast-fed. Physical examination, on admission, revealed marked jaundice of the skin with excoriations about the anus. The abdomen was distended and tympanitic, and the spleen was palpable below the costal margin. Blood could be seen oozing from the conjunctivæ. Rectal temperature was 99.6°. Laboratory studies showed the urine to be negative; hemoglobin, 50 per cent (Dare); red blood cells, 2,500,000 per c.mm.; white blood cells, 6200 per c.mm. Differential blood smear showed 33 per cent polymorphonuclears, 62 per cent lymphocytes, 2 per cent mononuclears, 2 per cent transitionals and 1 per cent eosinophils. Clotting time and bleeding time were each sixteen minutes, reduced in a week's time to a clotting time of eight minutes and a bleeding time of four minutes. The icterus index five days after admission was 84, and both direct and indirect van den Bergh reactions were positive. Intradermal tuberculin reaction was negative, as was the blood Wassermann. The platelet count was 160,000. A diagnosis of essential purpura hemorrhagica was made.

On the day of admission the patient was given 30 cc. of whole blood

* Reported through the courtesy of the Department of Pediatrics.

intramuscularly and 23 cc. of citrated blood intravenously. The temperature remained the same and the patient seemed improved, taking feedings regularly. On the third day after admission her temperature went to 102° and she lost weight in spite of feedings. A second blood transfusion of 75 cc. of citrated blood was given on the eighth day, but the child died the following day, August 5. There was no vomiting and no bleeding after the first blood was given. The jaundice seemed to deepen.

Postmortem Report. A necropsy was done immediately. It revealed marked emaciation, generalized jaundice, an enlarged spleen, atelectasis of the lower lobe of the right lung and a congenital anomaly of the cystic and hepatic ducts.

The entrance of the pancreatic duct into the bowel and the location and derivation of the cystic and hepatic arteries were normal. The common bile duct arose from the duodenum at its normal site (Fig. 1). At

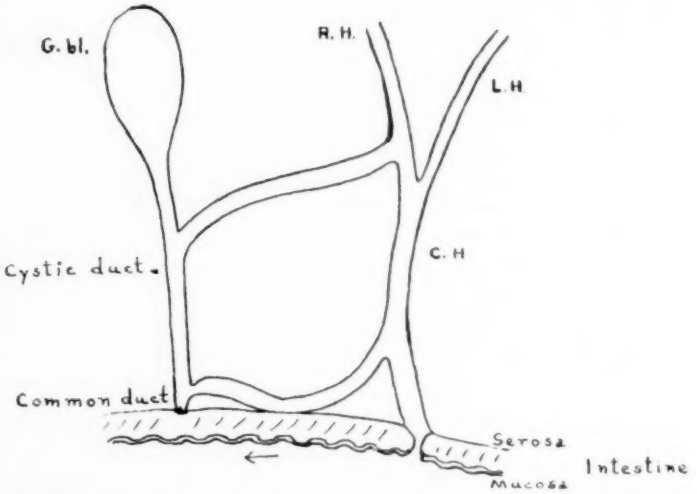

FIG. 1.—Diagrammatic sketch of the anomaly in this case. Arrow indicates the distal direction of the intestine.

a point 3 cm. above this site on the duodenum the common hepatic duct came off. These two vertical ducts were jointed by a horizontal duct which came off just above a constriction of the common duct. A second communicating duct was observed high up on the cystic duct, uniting with the right hepatic duct 1 cm. above the bifurcation of the common hepatic. The gall bladder was of normal infant size and color, containing a white mucoid material. Methylene blue injected into the right hepatic duct coursed down the communicating ducts and the common hepatic duct, and entered the duodenum. The gall bladder filled, but no dye entered the duodenum by way of the common duct. Microscopic sections showed acute and chronic pericholangitis.

An explanation of the embryologic mechanism underlying this anomaly may be of great interest. The normal development of the primary evaginations of the liver and pancreas is shown in the diagrammatic sketches of the reconstructions by Stoss (Fig. 2),

and Thyng (Fig. 3). The primary hepatic diverticulum is given off from the duodenum. It branches very early to produce the hepatic duct and the cystic duct, while the proximal end of the original diverticulum elongates to become the common bile duct.

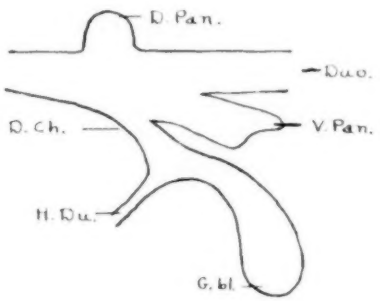

FIG. 2.—Diagram of model of the duodenum and the primary evaginations of the liver and pancreas in a 5-mm. sheep embryo. D. Pan., dorsal pancreas; V. Pan., ventral pancreas; Duo., duodenum; D. Ch., ductus choledochus; G. bl., gall bladder; H. Du., hepatic duct. (After Stoss.)

Soon after, the hepatic duct bifurcates. The gall bladder is formed later by expansion terminally of the cystic duct. Based upon the above reconstructions an attempt may be made to explain the anomaly found in this case.

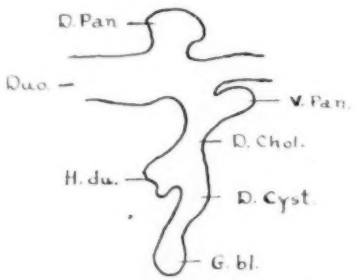

FIG. 3.—Diagram of reconstruction from human embryo, 7.5 mm., of primary evaginations of the liver and pancreas. D. Pan., dorsal pancreas; V. Pan., ventral pancreas; Duo., duodenum; D. Chol., ductus choledochus; G. bl., gall bladder; D. Cyst., ductus cysticus; H. du., hepatic duct. (After Thyng.)

The liver primordium given off from the duodenum failed to elongate normally during the initial stages, according to Jordan.[9] The gut in growing lengthwise appropriated the proximal undivided portion, thus effecting two separate entrances of the biliary ducts into the intestine (Fig. 4). The liver bud then began its normal growth and, due to the close proximity of the cystic and hepatic ducts, connecting branches between the hepatic and cystic ducts were formed from patent remains of earlier hepatic duct evagina-

tions which normally persist as the parietal sacculi of Beale in the wall of the hepatic duct. The gall bladder was formed normally by the dilatation of the distal end of the cystic duct. No definite

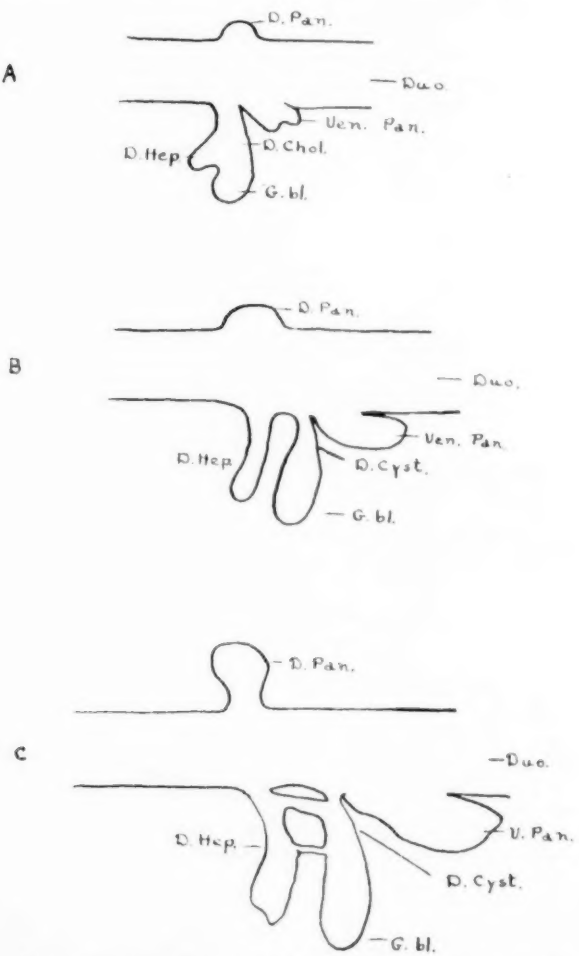

FIG. 4.—Diagrammatic sketch of probable development of the primary evaginations of the liver and pancreas in this case. D. Pan., dorsal pancreas; V. Pan., ventral pancreas; Duo., duodenum; D. Cyst., cystic duct; D. Hep., hepatic duct; G. bl., gall bladder. *A*, shows failure of liver bud to elongate. *B*, shows appropriation of proximal portion of bud by the growing gut, effecting separate entrances into the duodenum of the bile ducts; *C*, shows the connecting branches between the hepatic and cystic ducts being formed.

interpretation is put upon the failure of the common duct to become patent unless its occlusion is purely the result of a mechanical process.

This case presents three interesting features: the common duct and hepatic duct meet the duodenum at separate points, an abnormality of whose existence a surgeon should be cognizant; a communicating duct occurs as high as the cystic and right hepatic ducts; a constriction of the common duct causes its total occlusion. The first two features are of especial interest from an embryologic point of view.

Summary. A case is reported in which there are communicating ducts between the hepatic and cystic ducts, separate entrances of the common and hepatic ducts into the duodenum, and an occlusion of the common duct. It is presented as a probably unique congenital anomaly of the biliary tract. An attempt is made to explain the embryologic mechanism underlying this anomaly.

NOTE.—Since correcting the printer's proof of this article attention has been called to the article "Anomalous Bile Ducts in Man," by S. H. Mentzer, J. Am. Med. Assn., 1929, **93**, 1273. The anomaly described above resembles somewhat the normal anatomy in reptiles and some birds as reported by Mentzer.

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INTRAHEPATIC LITHIASIS.

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THE case herein reported is unusual in that: (1) The intrahepatic stones were much larger than any others hitherto encountered, according to the reports in the literature as far back as 1904;

(2) the patient's symptoms were meager considering the tremendous amount of stasis and consequent damage to the liver occasioned by the obstruction; (3) she recovered after operative removal.

Case Report. F. G., female, aged forty-five years, housewife, married, was admitted to the hospital on October 8, 1929, with the tentative diagnosis of chronic cholecystitis with cholelithiasis. The chief complaint was itching of the entire body, most marked at night, and pain in the right upper abdominal quadrant referred to the right shoulder. The present illness began about one month ago with itching of the entire body. At that time the itching was accompanied by pain in the upper right abdomen, with loss of appetite and some constipation. About three days before admission the patient was again seized with severe pain in the right upper abdomen. The sharp pain subsided and gave way to a dull ache over the same area. The stools were clay colored, the urine frothy and dark and there was a history of loss of weight of approximately 15 pounds in the last three months. Her past history and family history were entirely irrelevant to the present illness. On physical examination she appeared acutely ill, somewhat emaciated; temperature, 100.2°; pulse, 100; respirations, 26. The scleral conjunctivæ were jaundiced, and there was an icteric tint to the skin over the abdomen, chest and back. There was rigidity and tenderness over the right upper quadrant, most marked over the region of the gall bladder. Scratch marks were numerous. A slight umbilical hernia was noted. Varicosities of both lower extremities were present. With cholecystography the gall bladder failed to fill, but no stone shadows were detected. The Rosenthal-White liver function test revealed complete retention of the dye in the blood stream after thirty minutes.

Upon the diagnosis of cholecystitis and cholelithiasis with obstructive jaundice, she was subjected to operation the following day. The gall bladder was found to be distended and full of calculi. On palpation several stones were found free in the common duct and apparently not producing any obstruction or rather insufficient obstruction to account for the jaundice. The cystic duct was small and contained no calculi. At the point where the left hepatic duct emerged from the lower surface of the liver the end of a calculus was palpated. The hepatic duct at this point was markedly dilated. It was incised and a stone (*A*), 7 cm. long and 2 cm. in diameter, was removed from the intrahepatic portion of the left hepatic duct. Beyond this still more deeply embedded in the liver was another calculus, 4 cm. long by 2.5 cm. in diameter. Still deeper in the liver structure were many small calculi, varying in size. The right hepatic duct was likewise filled with these small calculi, which were removed through another incision. The incisions in the duct were closed around catheters sewn into both ends and extending deeply into the liver substance. The gall bladder was removed and the stones in the common duct were milked back through the stump of the cystic duct, which was then ligated. A cigarette drain was placed in the foramen of Winslow and the abdomen closed.

The patient had a rather stormy convalescence, necessitating a transfusion on October 14. The drainage from the abdominal wound through the catheters continued; the icterus gradually disappeared, and she was discharged on November 17 in a fairly good condition. When seen three months later the drainage from the abdominal wound had ceased entirely, the wound had healed completely and the patient was gaining weight and appeared in good physical condition. Six months later she developed moderate ascites. There was no edema of the extremities, or other sign of failing circulation. She still has moderate ascites.

Fig. 1, photographed to scale, represents the stones removed in this case. The color of the stones varied from a light yellow to a very dark brown. The large stone (*A*) was very firm in consistency, withstanding considerable rough handling in the operative removal from the intrahepatic portion of the duct. Its lower end was found to fit snugly against a smaller stone which was broken during removal, the fragments of which are represented by *B* and *C*. The smaller stones in the figure were all lying either behind the fragments *B* and *C* in the right hepatic duct or else in the left hepatic duct. All the calculi in this figure were removed from the intrahepatic portion of either the right or left hepatic duct. The gall bladder

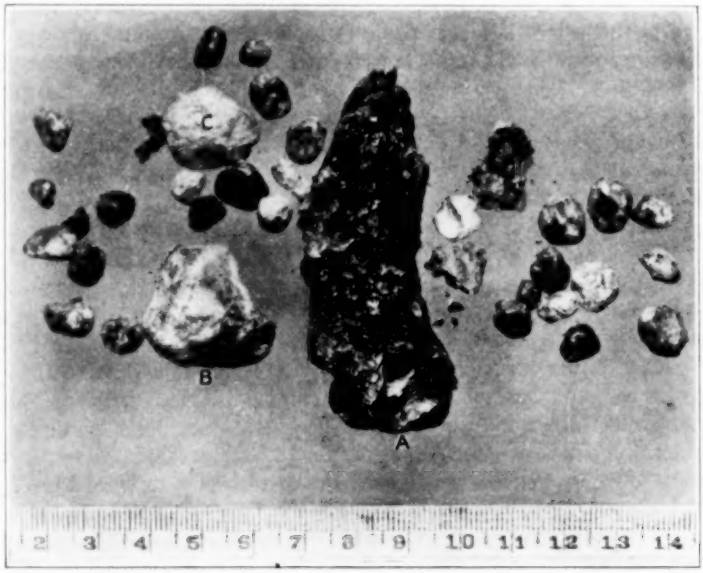

FIG. 1.—Large calculus *A* and smaller calculus represented by fragments *B* and *C*.

calculi and common duct calculi are not included in photograph. Fig. 2 represents a transverse section of the large stone. It is seen to consist of two portions, a cortex and medulla. In the center of the latter there is a fine cleft scarcely visible in the photograph. Cross section of the other small calculi also showed a cortical portion, a medullary portion and a central cleft that Aschoff terms the biliary calculus. Qualitative chemical analysis of the stones showed them all to consist of cholesterin, calcium and bilirubin pigment.

As the result of the accumulation of many individual experiences, the modern conception of the formation of gall stones has been

evolved, and this is set forth in as lucid a manner perhaps as is possible by Aschoff[1] in his "Lectures on Pathology." He classifies all gall stones in three divisions: metabolic stones, those due to infection and those due to stasis. The metabolic type is divided into two classes, one consisting purely of cholesterin and the other consisting of bilirubin. The former are always single, spherical and are found on cross section to consist of radiating crystals of cholesterin. When such a stone becomes impacted in the cystic duct, or when the gall bladder in which it is contained becomes the seat of an infection, the stone changes its character and becomes what is known as a combination stone, consisting of the central cholesterin nucleus, around which is deposited a shell of pigment, calcium and epithelial débris. Another type of metabolic stone is perhaps the pure pigment stone, which occurs in multiple and is ordinarily found in the gall bladder, usually mulberry shaped, rarely

FIG. 2.—Cross-section of large calculus (*A*) shown in Fig. 1.

oval or circular and never facetted. These stones are the size of a pea, hard, brittle, difficult to handle, very frequently disintegrating into coarse black sand. On cross section they present a metallic sheen, are sometimes brightly colored and are homogeneous without any layer formation and without any distinguishable nucleus or cortex. This stone can also be made into a combination stone by a superimposed infection with layering of cholesterin pigment and calcium.

The infectious type of stone is very characteristic. It occurs in two forms: the facetted calcium pigment cholesterin stone and the cylindrical calcium pigment cholesterin stone. The facetted cholesterin calcium stones are usually tetrahedral in shape. They have a soft, coarse nucleus, usually with more or less broad stellate branching, cleft projections of which reach to the cortex. The cortex is made up of numerous systems of lamellæ, and there is a very gradual transition from nucleus to cortex. The cortex is

harder than the nucleus; the nucleus is usually darker. The stones are usually all similar and very rarely is a second or third generation found from which one may conclude that all stones in a gall bladder have originated at one time and that they grow equally with every new inflammatory attack but that very rarely new stones arise.

The second form of infectious stone, the cylindrical or barrel shaped, has either a facetted surface, where it is in contact with other stones, or a nonfacetted, finely nodular surface, where it is in contact with the mucous membrane.

There is a third manner of gall stone formation in which stasis is the essential factor and which differs from the other two described, in that it takes place only in the bile passages. The resultant stones are composed of bilirubin and calcium. They are more or less soft, fragile, evenly colored, plainly laminated, red brown to brown black, sometimes egg shaped, sometimes round, sometimes sausage shaped or angular. They are most often found around foreign bodies, and the most important of these are gall bladder stones which have wandered away from the gall bladder. Thus we may have a gall bladder stone which has a new shell consisting of soft, earthy, bilirubin calcium rich in cholesterin. The nucleus may be that of any one of the stones previously described.

Infection is the factor which has been most under discussion in the literature. The relation of cholangitis to intrahepatic calculi is quite striking. Beer,[2] in a study of 250 livers of patients who had died of gall stone disease, found intrahepatic lithiasis in 6 cases, in all of which cholangitis was present. (It is interesting to note that these 6 cases also had extrahepatic calculi.) The degree of associated cholangitis varied from a mild catarrhal inflammation to a severe suppurative lesion. Courvoisier[3] found cholangitis in 15 out of 52 cases of stones in the hepatic duct or its branches. In reviewing Kehr's[4] report, Beer found 7 cases of intrahepatic lithiasis accompanied by cholangitis.

The elevation in the pulse rate, particularly in the presence of jaundice, the accelerated respirations and the accompanying rigidity and tenderness in the right upper quadrant are suggestive of some degree of infection of the biliary tract. The vicious cycle of stasis followed by infection and infection producing stasis has been repeatedly demonstrated in biliary disease. That dilatation of the extrahepatic and intrahepatic passages as far back as those of the fifth or seventh order is the invariable accompaniment of cholecystitis is also well known. With the tremendous dilatation and the complete obstruction of the ducts which occurred in our case it is surprising that there were not signs of grave infection of the tract.

Time Element in Stone Formation. The size of the stones found in our case brings up the question of the time element in their formation. Homens[5] found stones around a suture in the gall bladder in approximately one and a half years. Stones have been

produced experimentally in from three months to one year. The stones so produced were very small. It seems beyond belief that stones such as we described could have been formed in the one month of the patient's illness. Unquestionably these stones existed in the liver for a period of years, during which time she was apparently wholly free from symptoms. This is one of the most striking features of the case. Particularly is this true when one considers the tremendous handicap under which the patient must have been existing, as indicated by the liver function test. It furnished another example of the possibility for the symptomless existence of stones as long as there is no obstruction or severe infection.

Jaundice and Pain. Murchison,[6] in a discussion of intrahepatic calculi, states that they do not cause jaundice, and that they attain considerable size without giving pain. On the other hand, Rolleston[7] believes that all intrahepatic calculi are accompanied by some degree of icterus. That our patient was free from the symptoms of itching and jaundice for so long a period of time during which the stones must have been growing by accretion merely means that there never was a sufficiently complete obstruction to the bile flow. Even at the time of operation the jaundice was not very deep, although the stools were then already clay colored. Apparently the complete blockage was coincident with the onset of severe pain occurring three days before the operation. It probably did not result purely from a mechanical obstruction, but from a low-grade infection causing sufficient edema to completely close the lumen of the hepatic ducts. It is believed logical to conclude that the obstruction causing the icterus occurred here rather than in the common duct in which the small calculi were found to be freely movable.

In all the reported cases pain is the predominating symptom. Whether the pain is due to the intrahepatic or the extrahepatic calculi is a moot question. Again it is significant that, despite the large number and the large size of some of the calculi, pain did not become a factor until within a month of the time of operation.

Hepatitis Associated With Intrahepatic Lithiasis. Graham[8] and others have demonstrated the association of hepatitis with chronic cholecystitis. In a recent study of a large series of cases Koster, Goldzieher and Collens[9] confirmed this association, but also suggested, and presented some evidence in favor of the idea contrary to Graham's, that the liver lesion was secondary to and was dependent upon the lesion of the bile passages. While no section was taken from the liver of this patient, it seems hardly likely that it could have escaped a comparatively severe grade of secondary chronic infection. The liver function test showing complete retention of the dye in the blood is indicative of the altered functional state.

The presence of a small liver, found at the operating table, with

the recent development of ascites, not attributable to any other known cause, speaks for a development of cirrhosis of the liver in this patient. Although it is known that there is no direct connection between portal cirrhosis and hepatitis, the liver in this patient has suffered sufficient insult to produce a general intoxication by its altered function, and this may perhaps be said to be the cause of the onset of the ascites.

TREATMENT. The treatment is, of course, surgical, consisting of the removal of the stones and drainage of the ducts. While intrahepatic calculi are relatively rare, their recognition at operation will often depend upon the care with which the hepatic ducts are palpated during routine biliary tract surgery.

Summary. 1. A case of intrahepatic lithiasis is presented with unusually large-sized stones.

2. A striking feature of this case is the freedom from symptoms during the long period of time in which stone development undoubtedly occurred.

3. A discussion of the causes and associated features of stone development is presented.

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OBSERVATIONS ON THE CLINICAL APPLICATION OF THE URINE SEDIMENT COUNT (ADDIS).

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THE kidney, in common with other tissues, responds to inflammatory and degenerative processes by the elaboration of a more or less typical cellular reaction. These cellular elements eventually

find their way into the urine. It is reasonable then to conceive that a study of the formed elements in the urine may by their number and character indicate the type of structural change in the kidney from which they are derived. For example, in inflammatory disease mainly affecting the glomeruli, one would expect to find in the urine sediment a quantitative increase over the normal in the number of red blood cells as well as white blood cells. In degenerative lesions, one would expect to find a quantitative increase over the normal of epithelial cells desquamated from the renal tubules.

Haines and Skinner,[1] in 1898, showed that formed elements are present in the urine of normal persons. However, it fell to Addis[2] to establish the fact that the cellular elements of the urine are just as susceptible to quantitative estimation as those of the blood. In another study[3] he further showed that the urine sediment count might be employed to differentiate, on a purely clinical basis, the various types of Bright's disease.

We employed the urine sediment count in studying certain infectious diseases[4,5] and found it to be helpful.

Since congestive heart failure is not infrequently associated with certain forms of Bright's disease, we felt it was necessary to determine the influence of renal passive congestion alone, on the quantitative excretion of formed elements in the urine. No exact data on this question were found available in the literature.*

Furthermore, the clinical differentiation of active rheumatic carditis and subacute bacterial endocarditis occasionally offers much difficulty. We, therefore, also undertook to determine whether the sediment count, as a single added clinical fact, might be useful in this differentiation.

The technique for performing the urine sediment count was exactly as originally described by Addis.[3] On the day previous to the test the patient is asked to restrict fluid intake in order to submit a specimen of sufficient concentration to preserve hyalin casts.[3] Before retiring the bladder is completely emptied. Since the count is based on the 12-hour excretion, the specimen is best collected 12 hours after the last voiding. Where this is not possible a 6- or 9-hour specimen may be collected and a correction made in the calculation on the basis of a 12-hour excretion. Males void directly into the specimen bottle to prevent loss of any urine. Females must be catheterized to avoid contamination.† After carefully measuring the total volume voided it is thoroughly shaken

* Since this manuscript was prepared, the following study appeared: The Number of Formed Elements in the Urinary Sediment of Patients Suffering from Heart Disease, with Particular Reference to the State of Heart Failure. Stewart, H. J., and Moore, N. S.: J. Clin. Invest., December 20, 1930, **9**, 409.

† The collection of specimens for this quantitative procedure must be carried out with exactitude. The special nursing staff required was paid for in part from the funds of the Committee for Encouragement of Medical Research (Rheumatic Fever) and in part from the Crane Fund.

and 10 cc. placed in an Addis centrifuge tube.* This is centrifuged for fifteen minutes at about 1800 revolutions. After centrifuging, 9 cc. of supernatant urine is drawn off for the protein determination and the sediment is thoroughly mixed in the remaining 1 cc. When the sediment is heavy it may be mixed in 2 to 5 cc. of urine; when it is small in amount it is mixed in 0.5 cc. of urine and allowance made in the final calculation.

One drop of this sediment mixture is placed on a blood-counting chamber. Casts are counted with the low-power objective over the entire ruled area, representing a volume of 0.0009 cc. Red blood cells and white and epithelial cells are counted with the high-power objective over one small ruled area, representing a volume of 0.0001 cc. An average is taken of four to six different fields in the cast count and six to ten fields in the count of the other formed elements. A differential cast count is made at the same time as the total count.

From the average figures obtained in this way the calculation of the total 12-hour excretion rate of the formed elements is fairly simple. Addis has constructed a formula for this calculation.†

There are certain elements in the technique of this procedure which one acquires only after experience with the method. Casts must be distinguished from cylindroids. Red blood cells considered significant of glomerular origin are often faint, hemoglobinless rings or "ghosts," whereas red cells originating from somewhere in the genitourinary tract below the glomerulus are often sharply defined, biconcave and hemoglobin-filled. Since white blood cells are often indistinguishable from small round epithelial cells of the same approximate size derived from the tubules, they are counted together. However, Addis[3] noted that in glomerular inflammatory lesions white blood cells predominated over the epithelial cells in numbers, while in tubular degenerative lesions the reverse was true. Flat epithelium from the surface lining of the bladder and large round epithelium from the deeper layers of the genitourinary tract are not included in the count. The large variation in the count of these cells in normal persons may be accounted for by the inclusion of a number of these cells from the prostate and other glands of the genitourinary tract. However, Addis[3] showed that the count of these cells in the presence of an active renal lesion so far exceeds the usual count in persons without renal disease, as to make the standard set entirely satisfactory. It should be understood that this procedure is by no means meant to be strictly exact quantitatively

* These tubes may be obtained through Arthur H. Thomas Company, Philadelphia, U. S. A.

† $\text{Number counted} \times \frac{\text{vol. in cc. in which sediment was mixed}}{\text{vol. in cc. in which count was made}} \times \frac{\text{vol. in cc. per 12 hours}}{10}$

TABLE 1.—URINE SEDIMENT COUNT IN NORMAL PERSONS.

Number.	pH.	Sp. Gr.	Urine volume, cc. per 12 hrs.	Protein,* mg. per 12 hrs.	Red cells, millions per 12 hrs.	White and epithelial cells, millions per 12 hrs.	Casts,† thousands per 12 hrs.
1	5.0	1.030	369	5.3	0.0	0.22	9.2
2	5.0	1.040	259	18.0	0.0	0.064	0.0
3	5.0	1.031	473	10.2	0.0	0.118	0.0
4	5.5	1.023	355	12.78	0.0	0.117	0.0
5	5.0	1.044	208	8.9	0.0	0.062	0.0
6	5.0	1.020	616	22.1	0.0	0.077	0.0
7	5.5	1.010	776	8.38	0.0	0.580	0.0
8	5.0	1.027	228	32.8	0.0	0.3	3.8
9	5.8	1.027	408	57.7	0.0	0.73	0.0
10	5.5	1.027	269	23.12	0.0	0.67	2.2
11	6.7	1.032	186	26.8	0.0	0.6	4.1
12	5.6	1.028	337	24.8	0.0	0.4	0.0
13	5.0	1.036	147	.....	0.009	0.082	0.0
14	5.8	1.030	259	18.6	0.010	0.79	0.0
	5.7	1.028	234	16.8	0.26	1.1	7.8
15	5.5	1.028	285	42.0	0.01	0.81	3.2
16	5.0	1.040	158	5.6	0.013	0.115	0.0
17	5.5	1.018	145	10.4	0.02	0.29	2.2
18	5.0	1.035	170	18.3	0.02	0.36	0.0
19	5.0	1.028	80	5.75	0.022	0.52	0.0
20	5.5	1.032	335	21.7	0.027	1.36	
21	5.5	1.026	343	17.2	0.028	0.056	0.0
22	5.0	1.038	274	60.2	0.034	0.18	0.0
23	6.5	1.027	360	25.9	0.04	0.47	2.0
24	5.5	1.022	344	49.5	0.05	0.27	1.8
	5.0	1.027	186	26.6	0.09	0.72	1.03
25	5.5	1.036	226	26.18	0.06	0.19	0.0
26	5.8	1.029	239	29.3	0.07	0.37	0.0
27	5.7	1.020	363	52.2	0.07	0.7	2.0
28	5.0	1.032	287	15.4	0.071	0.262	0.0
29	6.5	1.024	387	13.9	0.072	0.097	0.0
30	5.0	1.034	137	2.9	0.076	0.34	0.0
31	5.3	1.034	220	.....	0.088	0.638	0.0
32	5.0	1.034	120	7.76	0.127	3.4	0.5
33	5.5	1.037	187	26.9	0.13	0.28	2.1
34	5.5	1.030	237	34.2	0.14	0.63	2.6
35	5.0	1.036	414	17.88	0.145	0.028	0.0
36	5.5	1.042	210	9.0	0.157	0.131	0.0
37	6.5	1.026	385	22.1	0.159	0.192	0.0
38	5.5	1.027	205	10.2	0.205	.....	0.0
39	6.0	1.031	312	33.7	0.16	0.81	0.0
	5.0	1.030	348	30.1	0.20	0.87	3.8
40	5.8	1.031	256	28.7	0.21	0.32	0.0
41	5.5	1.033	384	46.0	0.3	0.83	6.4
42	5.5	1.028	302	6.48	0.39	1.04	0.0
43	5.0	1.030	293	42.2	0.56	2.43	0.0
44	5.0	1.033	218	22.3	0.65	1.27	4.8
45	5.5	1.038	355	15.33	0.931	0.047	3.9
	5.0	1.043	280	10.0	1.53	0.024	0.0
Average	...	.....	...	21.8	0.146	0.540	1.29

* Centrifuge method (see reference 6).
† All were of hyalin variety.

and for clinical purposes need not be so, because in interpreting the sediment count one is concerned with numbers which often range in the hundreds of thousands, millions and in some instances billions. Likewise, sufficient leeway is allowed between the upper limit of normal counts and the lower limit of those considered abnormal.

Protein excretion was determined by the method described by Shevky and Stafford.[6]

Table 1 shows the results of forty-nine counts in 45 medical students in whom there was no reason to suspect past or present renal disease. It shows the average and range of variation in the 12-hour excretion rate of the formed elements. We have accepted as the upper limit of normal excretion in 12 hours: red blood cells, 500,000; white blood cells and epithelial cells, 1,000,000; casts, 5000. With very few exceptions, these figures are well above the upper range and considerably above the observed averages. The "normal" limits we have set were exceeded only four times in the "normal" cases, by the red blood cells, twice by the white blood cells and three times by the casts. While one may wish to apportion our normal upper limits somewhat differently, it is well to remember that exact figures are almost impossible of attainment. Also, that the entire procedure must be accepted as only a single added clinical fact and its usefulness is dependent upon its correlation with other available clinical data.

Table 2 serves to indicate that the diagnosis of microscopic hematuria may be impossible unless the urine volume is taken into consideration as well as the concentration of the formed elements to be counted.

TABLE 2.—THE VALUE OF THE URINE SEDIMENT COUNT IN THE DIAGNOSIS OF MICROSCOPIC HEMATURIA.

Urine volume, cc. per 12 hrs.	No. of R. B. C. in 10 H. P. F. (concentration).	Twelve-hour output of R. B. C. in urine (excretion rate).	Interpretation.
100	1.0	160,000	Normal
200	1.0	320,000	Normal
1,000	1.0	1,600,000	Hematuria
2,000	1.0	3,200,000	Hematuria

In Table 3 are listed nineteen quantitative counts of the formed elements in the urine sediment of 10 patients with acute, subacute and chronic glomerulonephritis. Since it was of great importance for our present purpose to be certain of the diagnosis in these patients, due precautions were taken to choose a selected group. The diagnosis of glomerulonephritis in Patients 3 and 5 was confirmed by necropsy. Patient 1 developed edema, hypertension and renal insufficiency under our observation, while convalescing from lobar pneumonia. The rest of this group consisted of patients with azotemia or marked renal insufficiency and anemia, as well as the history and usual clinical course of glomerulonephritis.

TABLE 3.—STUDY OF THE TWELVE-HOUR EXCRETION RATE OF FORMED ELEMENTS IN THE URINE OF PATIENTS WITH DIFFUSE GLOMERULONEPHRITIS.

Name.	No.	Date.	Urine volume, cc. per 12 hrs.	pH.	Specific gravity.	Protein, mg. per 12 hrs.	R. B. C. in millions per 12 hrs.	White and epithelial cells in millions per 12 hrs.	Casts per twelve hours in thousands.				
									Total.	Hyalin.	Granular.	W. B. C. and epithelial.	Blood.
A	1	4/ 9/30	143	5.0	1.010	2162	13.41	5.18	1120	1000	120	0	0
		4/12/30	251	5.0	1.013	2349	37.37	7.91	2649	149	2500	0	0
		5/15/30	1520	5.0	1.007	4370	1157.0	0.15	0	0	0	0	0
		6/11/30	473	5.5	1.007	683	299.0	45.44	972	72	900	0	0
		7/30/30	....	..	1.011	....	115.6	8.82	350				
D	2	3/ 9/30	746	5.0	1.010	7520	490.49	33.57	11605	11605	0	0	0
F	3	1/20/30	980	5.0	1.016	8050	20.58	36.06	971	485	480	6	0
G	4	12/11/29	578	5.5	1.015	12484	38.0	0.94	0	0	0	0	0
S	5	10/ 1/29	798	5.0	1.020	5460	44.7	15.96	5320	320	5000	0	0
		10/16/29	826	5.0	1.024	8326	32.2	8.67	12711	711	12000	0	0
B	6	6/24/30	325	5.5	1.010	76	3.76	2.6	966	800	123	43	0
R	7	9/ 9/30	514	5.0	1.011	384	8.89	10.95	14	14	0	0	0
		9/26/30	492	6.8	1.010	45	41.20	3.30	150	125	0 3	25	0
C	8	9/ 9/30	585	7.4	1.012	273	4.97	107.4	194	194	0	0	0
		9/15/30	677	7.5	1.010	146	13.80	47.7	0	0	0	0	0
M	9	9/30/30	195	6.8	1.014	31	46.41	1.2	173	173	0	0	0
		10/ 4/30	295	5.0	1.018	148	43.0	2.9	82	82	0.5	0	0
		10/23/30	576	5.0	1.012	321	27.8	2.0	55	55	0.5	0	0
Ca	10	10/28/30	822	7.5	1.004	....	2.88	4.1	22	22	0	0	0

TABLE 4.—STUDY OF THE TWELVE-HOUR EXCRETION RATE OF FORMED ELEMENTS IN THE URINE OF PATIENTS WITH CONGESTIVE HEART FAILURE.

Name.	No	Date.	Urine volume, cc. per 12 hrs.	pH.	Specific gravity.	Protein, mg. per 12 hrs.	R. B. C. in millions per 12 hrs.	White and epithelial cells in millions per 12 hrs.	Casts per twelve hours, in thousands.				
									Total.	Hyalin.	Granular.	W. B. C. and epithelial.	Blood.
Ba	1	2/24/30	373	5.0	1.012	393	0.31	18.64	213	172	27.5	13.5	0
		4/29/30	198	5.5	1.015	206	0.2	9.56	687	655	32.5	0	0
Ca	2	11/16/29	955	7.0	1.020	343	0.0	0.95	0	0	0	0	0
Cb	3	7/20/29	222	5.0	1.030	411	0.04	0.64	144	83	61.7	0	0
Da	4	2/ 1/30	194	5.0	1.028	2880	0.25	2.18	3915	3740	108	67.5	0
Fa	5	10/ 9/29	524	5.5	1.016	113	0.0	0.26	0	0	0	0	0
		10/17/29	189	5.0	1.032	231	0.0	1.56	183	157	26.3	0	0
		11/ 5/29	1712	5.5	1.006	61	0.21	41.94	166	166	0	0	0
Fb	6	11/26/29	400	5.0	1.034	2016	0.42	0.42	19	19	0	0	0
		12/ 3/29	470	5.0	1.030	186	0.18	1.29	19	19	0	0	0
Ga	7	11/ 1/29	238	5.0	1.014	15	0.11	0.06	0	0	0	0	0
Gb	8	10/ 3/29	252	5.0	1.032	36	0.0	0.15	336	245	91	0	0
		10/ 9/29	192	5.0	1.030	45	0.0	0.1	48	29	18.6	0	0
		10/21/29	46	5.0	1.030	49	0.01	0.18	23	21	2	0	0
Ja	9	2/25/30	123	5.0	1.022	39	0.03	3.07	43	26	17	0	0
La	10	1/18/30	131	5.0	1.034	330	0.02	1.83	0	0	0	0	0
Ma	11	2/ 5/30	273	5.5	1.025	484	0.07	3.03	47559	47500	0	59	0
Oa	12	10/ 4/29	332	5.0	1.026	143	0.21	0.58	0	0	0	0	0
Ob	13	10/15/29	735	5.5	1.022	105	0.0	4.23	81	40	40.8	0	0
Pa	14	2/26/30	347	5.0	1.015	2998	0.65	1.21	192	192	0	0	0
Ra	15	9/11/29	206	5.0	1.028	29	0.10	1.66	0	0	0	0	0
		10/ 1/29	464	5.0	1.022	128	0.0	1.28	0	0	0	0	0
Sa	16	11/12/29	296	5.0	1.028	42	0.04	0.81	16	16	0	0	0
		3/ 9/30	348	5.0	1.010	225	2.61	0.52	104	34	0	70	0
Sb	17	10/ 4/29	1062	6.5	1.012	229	0.93	45.14	13	13	0	0	0
Gc	18	5/16/30	609	5.0	1.011	153	0.0	1.98	0	0	0	0	0
Ha	19	4/28/30	396	5.0	1.021	2708	0.97	6.24	2342	1753	587.5	0	0
Wa	20	4/28/30	507	5.5	1.020	1825	0.25	1.9	9604	9100	504.8	0	0
L	21	1/15/30	427	5.5	1.030	123	0.12	1.71	0	0	0	0	0
		1/28/30	395	5.0	1.024	85	0.53	0.33	0	0	0	0	0
		2/ 4/30	288	5.0	1.025	58	0.32	0.25	0	0	0	0	0
S	22	9/11/30	450	5.8	1.020	81	0.07	1.12	140	140	0	0	0
M	23	9/17/30	200	5.5	1.024	43	0.15	2.44	0	0	0	0	0
		10/ 8/30	164	5.5	1.020	153	0.66	1.77	152	152	0	0	0
T	24	10/ 4/30	440	5.0	1.020	216	0.44	27.72	122	122	0	0	0
H	25	10/ 8/30	288	5.0	1.030	88	0.86	43.20	1942	1400	542	0	0
Ha	26	10/ 9/30	246	5.0	1.016	283	0.57	8.36	410	410	0	0	0
		10/28/30	240	6.8	1.015	...	0.56	123.8	0	0	0	0	0

In Table 4 the same observation is repeated thirty-eight times in 26 patients with congestive heart failure. While the excretion rate of protein, white and epithelial cells and casts is comparable in both conditions, there is a striking difference in the excretion rate of red blood cells. In active glomerulonephritis microscopic hema-

TABLE 5.—QUANTITATIVE STUDY OF THE TWELVE-HOUR URINE SEDIMENT COUNT IN ACUTE RHEUMATIC INFECTION.

Name	No.	Date.	Urine volume, cc. per 12 hrs.	pH.	Specific gravity.	Protein, mg. per 12 hrs.	R. B. C. in millions per 12 hrs.	White and epithelial cells in millions per 12 hrs.	Casts per twelve hours, in thousands.					Temperature, °F.
									Total.	Hyalin.	Granular.	Epithelial.	Blood.	
Aa	1	4/ 8/30	310	5.0	1.021	89	0.00	3.23	0	0	0.0	0.0	0.0	99.4
Ba	2	5/ 2/29	513	5.0	1.024	2954	3.00	28.00	6000	6000	0.0	0.0	0.0	103.4
		5/14/29	358	5.5	1.032	25	5.75	32.76	14	14	0.0	0.0	0.0	99.6
		5/15/29	255	5.5	1.034	18	4.03	6.82	21	21	0.0	0.0	0.0	100.2
		5/29/29	605	6.0	1.024	13	0.69	3.73	36	36	0.0	0.0	0.0	99.8
		6/ 4/29	1174	6.5	1.024	50	0.73	3.52	0	0	0.0	0.0	0.0	98.4
		7/31/29	303	5.0	1.030	15	0.35	1.59	2	2	0.0	0.0	0.0	98.6
		11/22/29	308	5.5	1.020	60	0.25	0.10	0	0	0.0	0.0	0.0	98.6
Bb	3	4/16/29	464	6.5	1.030	33	0.75	0.46	0	0	0.0	0.0	0.0	101.0
Ca	4	1/25/30	70	5.0	1.018	22	0.003	1.82	0	0	0.0	0.0	0.0	102.6
Cd	5	5/11/29	300	5.5	1.030	32	1.20	5.00	217	176	41.0	0.0	0.0	103.4
		5/15/29	255	5.0	1.030	16	0.77	2.87	0	0	0.0	0.0	0.0	103.4
		5/21/29	552	5.5	1.034	50	14.64	531.46	0	0	0.0	0.0	0.0	102.4
		6/ 5/29	458	5.5	1.016	92	3.21	292.97	0	0	0.0	0.0	0.0	103.2
		6/14/29	238	5.0	1.022	15	0.06	22.68	6	6	0.0	0.0	0.0	100.0
		7/18/29	88	5.0	1.026	38	0.03	0.38	2	2	0.0	0.0	0.0	99.0
Da	6	2/ 6/30	600	5.5	1.024	2100	36.00	5.10	16	0	0.0	0.0	16.6	102.2
		2/17/30	828	5.0	1.012	59	2.38	1.55	23	23	0.0	0.0	0.0	101.8
		2/22/30	580	5.0	1.012	41	2.32	1.16	8	8	0.0	0.0	0.0	102.2
		3/ 6/30	607	5.0	1.012	43	1.12	1.67	0	0	0.0	0.0	0.0	99.6
Db	7	4/30/29	404	5.5	1.022	37	0.50	3.00	0	0	0.0	0.0	0.0	104.2
		5/ 8/29	348	5.5	1.027	50	0.70	1.00	60	34	26.0	0.0	0.0	100.0
		5/22/29	312	5.0	1.016	28	0.61	0.39	33	33	0.0	0.0	0.0	99.4
		6/ 3/29	210	5.0	1.036	15	0.00	0.37	49	35	14.3	0.0	0.0	99.6
		6/11/29	374	5.0	1.032	26	0.23	0.65	62	62	0.0	0.0	0.0	99.6
		6/17/29	320	5.5	1.036	18	0.16	0.44	53	53	0.0	0.0	0.0	99.2
		6/26/29	270	5.5	1.036	15	0.03	0.27	22	22	0.0	0.0	0.0	98.8
Dc	8	3/12/29	220	5.0	1.030	trace	0.60	1.00	24	21	0.0	3.0	0.0	101.8
		3/28/29	387	5.0	1.030	54	0.30	0.90	0	0	0.0	0.0	0.0	99.8
		4/ 8/29	398	5.0	1.030	14	0.30	0.15	0	0	0.0	0.0	0.0	100.0
		4/13/29	265	5.0	1.025	48	0.40	0.50	0	0	0.0	0.0	0.0	99.4
		4/20/29	303	5.0	1.030	21	0.50	0.30	0	0	0.0	0.0	0.0	99.6
Dd	9	11/29/29	236	5.5	1.036	17	0.00	0.24	0	0	0.0	0.0	0.0	101.8
		12/ 3/29	244	5.5	1.032	17	0.06	0.20	0	0	0.0	0.0	0.0	99.0
		12/30/29	186	5.0	1.020	13	0.00	0.02	0	0	0.0	0.0	0.0	98.6
		2/11/30	225	5.0	1.020	0	0.52	0.03	0	0	0.0	0.0	0.0	99.0
		4/ 7/30	267	5.5	1.017	15	0.09	0.00	0	0	0.0	0.0	0.0	99.0
De	10	4/24/29	582	5.0	1.026	111	5.00	1.00	366	86	45.0	65.0	0.0	101.0
		5/ 6/29	590	5.0	1.024	42	0.74	7.00	196	17	162.0	17.0	0.0	99.6
		5/14/29	640	5.5	1.024	32	0.16	2.62	160	160	0.0	0.0	0.0	98.6
		5/23/29	760	5.0	1.020	19	0.38	1.42	63	63	0.0	0.0	0.0	99.2
		6/ 3/29	540	5.0	1.028	18	0.24	2.12	60	60	0.0	0.0	0.0	99.2
		6/11/29	385	5.5	1.014	12	0.00	0.11	6	6	0.0	0.0	0.0	98.0
		8/ 8/29	500	5.5	1.026	25	0.13	0.56	0	0	0.0	0.0	0.0	98.0
Fa	11	3/13/29	270	5.5	1.032	15	0.09	0.19	12	4	4.0	4.0	0.0	99.0
		3/21/29	385	5.5	1.030	13	0.14	0.50	10	10	0.0	0.0	0.0	99.0
Ha	12	3/18/29	447	5.5	1.040	0	1.40	1.00	51	0	34.0	23.0	0.0	101.0
		3/27/29	107	5.0	1.040	50	0.20	2.00	2	0	0.0	0.0	0.0	100.0
		4/ 5/29	413	5.0	1.028	29	2.00	12.00	15	0	7.7	7.7	0.0	100.8
		4/12/29	325	5.0	1.040	35	4.00	11.00	0	0	0.0	0.0	0.0	100.0
		4/19/29	790	5.0	1.024	39	0.50	4.00	0	0	0.0	0.0	0.0	99.8
		5/17/29	470	5.5	1.020	50	3.70	6.29	6	6	0.0	0.0	0.0	99.6
		5/24/29	410	5.0	1.030	29	1.72	0.41	11	0	11.4	0.0	0.0	98.2
		6/1 /29	600	5.0	1.028	32	0.12	0.64	100	100	0.0	0.0	0.0	98.1
		6/13/29	783	5.0	1.020	16	0.39	0.29	87	87	0.0	0.0	0.0	99.2
		6/17/29	548	5.5	1.022	17	0.34	0.48	38	38	0.0	0.0	0.0	99.2
		6/26/29	230	5.0	1.042	13	0.64	1.34	97	97	0.0	0.0	0.0	99.2

TABLE 5.—QUANTITATIVE STUDY OF THE TWELVE-HOUR URINE SEDIMENT COUNT IN ACUTE RHEUMATIC INFECTION—(*Continued*).

Name	No.	Date.	Urine volume, cc. per 12 hrs.	pH.	Specific gravity.	Protein, mgm. per 12 hrs.	R. B. C. in millions 12 hrs.	White and epithelial cells in millions per 12 hrs.	Casts per twelve hours, in thousands.					Temperature, °F.
									Total.	Hyalin.	Granular.	Epithelial.	Blood.	
Ka	13	11/13/29	788	5.0	1.026	532	1.75	1.36	86	21	65.2	0.0	0.0	103.0
		11/27/29	240	5.5	1.036	17	0.36	0.27	0	0	0.0	0.0	0.0	102.2
		12/3/29	330	5.0	1.034	83	0.21	0.83	18	9	9.1	0.0	0.0	100.2
		12/28/29	658	5.5	1.016	47	0.08	0.74	36	27	0.0	9.1	0.0	99.0
		2/18/30	506	5.0	1.022	124	0.75	0.51	0	0	0.0	0.0	0.0	99.2
		3/5/30	247	5.0	1.026	53	1.58	0.07	3	3	0.0	0.0	0.0	98.6
La	14	3/13/29	364	5.5	1.032	trace	9.00	2.00	7	0	0.0	7.0	0.0	100.4
		3/16/29	804	5.0	1.025	trace	2.60	2.80	78	22	55.6	0.0	0.0	101.0
		3/27/29	253	5.0	1.032	36	0.60	0.50	0	0	0.0	0.0	0.0	98.8
		4/5/29	368	5.5	1.030	13	0.40	1.50	0	0	0.0	0.0	0.0	99.0
		4/29/29	423	5.0	1.030	176	2.80	7.00	47	31	0.0	15.5	0.0	99.0
		5/6/29	350	5.0	1.026	35	0.18	1.00	0	0	0.0	0.0	0.0	99.0
		5/29/29	262	5.5	1.034	5	0.06	0.02	0	0	0.0	0.0	0.0	99.6
Lb	15	3/20/29	153	6.0	1.028	10	0.60	0.80	0	0	0.0	0.0	0.0	102.4
		4/1/29	318	6.0	1.030	20	0.40	2.00	0	0	0.0	0.0	0.0	101.0
		4/9/29	594	5.5	1.030	64	2.50	42.00	0	0	0.0	0.0	0.0	99.8
		4/17/29	535	5.0	1.032	26	0.50	8.00	0	0	0.0	0.0	0.0	98.6
		5/21/29	410	5.5	1.022	44	0.20	2.87	0	0	0.0	0.0	0.0	98.4
Ma	16	5/14/29	216	5.0	1.018	1162	0.05	2.20	1080	108	972.0	0.0	0.0	104.0
		6/10/29	152	5.0	1.038	455	1.42	4.19	52	52	0.0	0.0	0.0	99.4
		7/17/29	380	5.0	1.026	8	0.53	3.69	100	100	0.0	0.0	0.0	99.4
Mb	17	3/16/29	388	5.0	1.034	0	0.78	0.97	0	0	0.0	0.0	0.0	100.8
		4/3/29	435	5.5	1.030	93	4.50	0.30	0	0	0.0	0.0	0.0	100.0
		4/8/29	580	5.5	1.020	8	17.00	0.60	0	0	0.0	0.0	0.0	99.4
		4/13/29	530	5.5	1.030	38	10.40	0.46	0	0	0.0	0.0	0.0	98.6
Mc	18	3/19/29	376	5.0	1.030	0	10.40	0.60	22	8	8.8	4.4	0.0	102.0
		3/28/29	400	5.0	1.024	57	0.50	0.50	44	26	13.2	4.4	0.0	99.8
		4/9/29	373	5.5	1.020	26	0.80	0.25	93	70	20.0	3.0	0.0	100.0
		4/17/29	817	5.8	1.020	58	0.50	0.70	22	22	0.0	0.0	0.0	100.6
Na	19	4/23/29	258	5.0	1.032	2600	1.60	1.00	86	0	86.0	0.0	0.0	104.6
		5/7/29	261	5.0	1.030	60	1.60	2.00	29	0	29.0	0.0	0.0	100.0
		5/16/29	390	6.5	1.020	20	0.30	0.40	103	27	76.0	0.0	0.0	99.5
		5/24/29	698	5.0	1.024	49	1.14	1.15	209	209	0.0	0.0	0.0	99.0
		6/1/29	760	6.5	1.023	38	0.43	0.43	84	84	0.0	0.0	0.0	99.2
		6/7/29	587	6.0	1.022	42	0.63	0.83	0	0	0.0	0.0	0.0	99.0
		6/13/29	570	5.5	1.024	16	0.93	0.42	31	23	7.9	0.0	0.0	99.0
		7/18/29	705	5.0	1.020	26	0.06	0.39	11	11	0.0	0.0	0.0	99.0
Oa	20	2/19/30	348	5.0	1.022	37	0.25	2.75	1	1	0.3	0.0	0.0	99.6
Pa	21	3/18/29	1350	5.5	1.012	mod.	5.00	13.00	30	0	22.5	7.5	0.0	103.6
		3/26/29	604	5.0	1.020	34	3.00	8.00	39	19	15.8	4.2	0.0	102.0
		4/2/29	536	6.0	1.026	57	0.26	0.34	0	0	0.0	0.0	0.0	102.0
		4/25/29	367	5.0	1.030	36	0.50	3.50	56	14	42.0	0.0	0.0	99.4
		5/11/29	213	5.0	1.030	15	0.20	0.90	15	9	3.0	3.0	0.0	98.6
Pb	22	2/20/30	564	5.0	1.022	60	1.83	8.87	0	0	0.0	0.0	0.0	101.4
		3/7/30	716	5.5	1.016	103	0.72	1.43	79	59	19.9	0.0	0.0	99.6
Ra	23	2/27/30	337	5.0	1.024	15	2.02	26.79	0	0	0.0	0.0	0.0	103.4
Rb	24	2/10/30	58	5.0	1.026	83	0.80	0.17	0	0	0.0	0.0	0.0	104.2
		2/26/30	644	5.5	1.015	69	0.24	2.66	0	0	0.0	0.0	0.0	99.2
		3/6/30	349	5.0	1.015	25	1.45	1.53	0	0	0.0	0.0	0.0	99.4
		3/13/30	460	5.0	1.011	49	0.92	1.73	0	0	0.0	0.0	0.0	99.6
Rc	25	2/10/30	494	6.0	1.016	105	0.06	0.37	6	6	0.0	0.0	0.0	103.0
		3/5/30	135	5.0	1.021	19	0.07	1.22	15	15	0.0	0.0	0.0	101.8
Sa	26	4/25/30	745	5.0	1.018	107	0.25	53.83	20	20	0.0	0.0	0.0	104.0
		5/22/30	2100	5.0	1.007	77	0.00	2.38	192	192	0.0	0.0	0.0	100.6
Sb	27	2/5/30	562	5.0	1.016	121	2.39	7.03	68	54	0.0	13.6	0.0	99.8
Sc	28	3/11/29	1245	5.0	1.012	0	0.20	0.45	76	55	14.0	7.0	0.0	99.6
Ta	29	4/16/29	303	6.5	1.040	872	5.50	1.35	0	0	0.0	0.0	0.0	105.6
		4/20/29	654	5.5	1.030	882	11.00	3.00	0	0	0.0	0.0	0.0	103.0
		5/1/29	413	5.5	1.030	29	1.50	8.00	23	11	11.5	0.0	0.0	99.6
Ua	30	3/21/29	315	5.0	1.035	34	0.50	1.0	35	8	26.3	0.0	0.0	101.6
		4/2/29	587	6.0	1.022	63	0.60	1.00	0	0	0.0	0.0	0.0	101.0
		4/11/29	385	5.5	1.030	8	0.30	7.00	59	21	26.8	10.8	0.0	102.0
		4/18/29	425	5.0	1.030	30	0.30	4.50	12	6	6.0	0.0	0.0	102.0
Wa	31	3/19/29	445	5.0	1.024	0	0.10	1.00	74	37	24.7	12.3	0.0	103.6
		4/4/29	323	5.0	1.036	34	2.20	2.50	0	0	0.0	0.0	0.0	99.6
		4/11/29	400	5.0	1.030	43	0.30	0.55	44	11	33.0	0.0	0.0	99.0

turia was present in each examination. It was persistent where counts were repeated and often of marked degree. However, in the renal passive congestion microscopic hematuria (upper limit of normal red blood cell excretion taken as 500,000 per 12 hours) occurred only six times in thirty-eight determinations. In each instance it was mild in degree, and when counts were repeated (on 2 patients) the hematuria was found not to be persistent. The clinical differentiation of renal inflammation of glomerulonephritis and renal passive congestion of hypertensive heart failure is often most difficult and occasionally quite impossible. In both instances there may be hypertension, cardiac enlargement, edema and moderate rise in the blood urea nitrogen. A qualitative analysis of a casual or 24-hour urine specimen may leave one with the impression that both sediments are of similar character in regard to formed element content. (Table 2.) However, a quantitative study of the urine sediment, as we have shown, will reveal the presence or absence of microscopic hematuria. While it is true that occasionally one sees glomerulonephritis without demonstrable microscopic hematuria, it must be remembered that the urine sediment count is not of itself diagnostic, but rather added fact which must be considered in the light of other correlated clinical data.

Table 5 represents a series of 31 patients with acute rheumatic infection investigated with the urine sediment count.[4]

TABLE 6.—STUDY OF THE TWELVE-HOUR EXCRETION RATE OF FORMED ELEMENTS IN THE URINE OF PATIENTS WITH SUBACUTE BACTERIAL ENDOCARDITIS.

Name	No.	Date	Urine volume, cc.	pH.	Specific gravity.	Protein, mg. per 12 hrs.	R. B. C. in millions per 12 hrs.	White and epithelial cells in millions per 12 hrs.	Casts per twelve hours, in thousands.					Temperature, °F.
									Total.	Hyalin.	Granular.	W. B. C.	Blood.	
Ca	1	5/29/30	514	5.0	1.020	277	1.8	4.24	3198	240	2958.0	0.0	0.0	103.0
Cb	2	5/17/30	420	5.0	1.020	453	52.92	5.04	151	151	0.0	0.0	0.0	100.0
E	3	1/3/30	131	5.0	1.027	28	0.56	0.56	12	8	2.1	2.1	0.0	103.0
H	4	1/18/30	410	5.5	1.014	410	44.28	3.69	273	273	0.0	0.0	0.0	101.6
K	5	1/15/30	309	5.5	1.016	411	68.36	23.64	103	0	28.0	75.0	0.0	101.6
		1/20/30	390	5.0	1.015	250	9.24	12.84	542	195	195.0	152.0	0.0	104.0
T	6	1/15/30	1180	5.0	1.014	629	11.51	5.55	277	179	33.0	65.0	0.0	100.8
		6/12/30	1340	5.5	1.007	578	24.34	4.65	74	74	0.0	0.0	0.0	
W	7	9/29/30	364	5.0	1.024	915	5.09	3.39	222	222	0.2	0.0	0.0	
K	8	9/12/30	804	6.5	1.017	184	142.31	11.26	279	179	0.0	75.0	25.0	

Table 6 shows the same observation in 8 patients with proven subacute bacterial endocarditis. Again a striking difference is noted, only in the degree of microscopic hematuria. Not infrequently the differential diagnosis between acute rheumatic carditis and subacute bacterial endocarditis is difficult at certain stages of the disease. It appears from our observations that the occurrence of persistent and well-marked microscopic hematuria along with the other clinical manifestations favors the latter diagnosis. The

occurrence of hematuria in subacute bacterial endocarditis is well known, and frank renal bleeding which may occur even in the absence of visible embolic phenomena, is highly suggestive of the diagnosis. However, the recognition of moderate degrees of microscopic hematuria which, if persistent, are just as significant, are often extremely difficult of recognition unless one resorts to an actual quantitative estimation.

Summary. The method for performing the urine sediment count (Addis) has been described in groups of: (1) "Normal" individuals (45); (2) patients with nephritis (10); (3) patients with congestive heart failure (26); (4) patients with acute rheumatic fever (23); (5) patients with subacute bacterial endocarditis (8).

The advantage in certain instances of a quantitative study of the formed elements in the urine sediment over the usual qualitative method of study has been indicated. It has been shown that the application of this more exact quantitative procedure may be of aid in making certain differential diagnoses.

Conclusions. 1. Healthy individuals in a 12-hour period may excrete up to 500,000 red blood cells, 1,000,000 white and epithelial cells and 5000 casts.

2. "Hematuria" is unusual as a result of renal passive congestion alone.

3. Subacute bacterial endocarditis is the only form of heart disease in which striking hematuria may occur.

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DISTURBANCES IN HANDWRITING AND CLUMSINESS AS SIGNS OF TOXIC GOITER.

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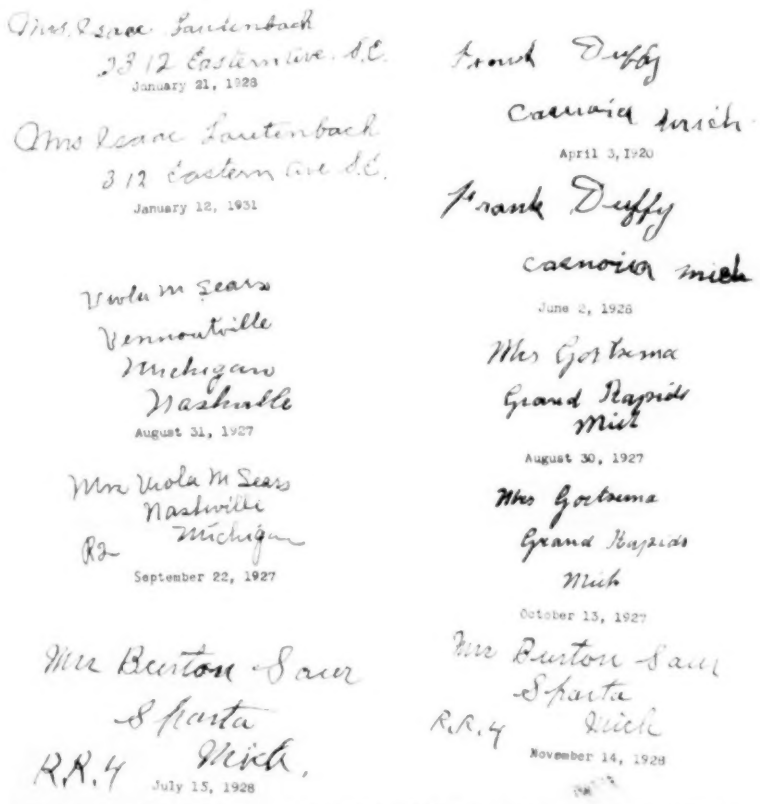
At a recent medical meeting a statement was made by a nationally known neurologist that tremor of toxic goiter does not affect one's handwriting. This statement surprised me in view of my own

observations and studies of this phase of tremor of thyrotoxic origin. I found a similar, but somewhat modified statement by Jackson:[1] "The tremor is so fine that it does not materially affect the handwriting or cause a patient to spill a glass of water."

In obtaining a history 3 or 4 years ago from a patient at the time definitely toxic, a statement was volunteered that his first observation of anything wrong was in having trouble with the handwriting. While this was only an expression of tremor of the fingers and



The handwriting of 5 cases of toxic goiter before and after surgical treatment.

hands, it nevertheless was interesting. Other toxic goiter patients were then asked if there was any disturbance in their handwriting, and it was quite surprising to note how many had been so troubled. A number of specimens of handwriting were then gathered, both before and after their surgical treatment. (See illus.) They demonstrated that the handwriting may be very definitely affected as a result of the tremor that is a part of their toxicity. One patient volunteered the statement that the first intimation of a change in

his condition was that he observed some difficulty in shaving because of the tremor of his hands, a similar manifestation, of course. Jackson's reference to not spilling a glass of water further interested me because it is at variance with my experience. Patients have voluntarily mentioned being "clumsy." They drop their glasses, or dishes, or anything they may be handling.

Tremor is known to be one of the cardinal symptoms and signs of Graves' disease. It is also one of the earliest. It may be present for months before the disease is fully developed. The sign may first manifest itself as interference with fine work, as, for example, a woman doing needlework, or an artisan performing whatever kind of work in which he may be engaged. In other words, it is obvious that the tremor would be observed, if at all, by one doing fine work. Why should not tremor also affect one's handwriting? Tremor is, of course, not pathognomonic of Graves' disease, since it is also found in various other conditions, both functional and organic. The purpose of this note is not to discuss the entire subject of tremor, but merely to show that disturbances in handwriting, also "clumsiness," may obtain in goiter toxicity, when, if recognized, they may be the hint of the existence of an early or mild case of Graves' disease.

REFERENCE.

1. Jackson, A. S.: Goiter and Other Diseases of the Thyroid Gland, Paul B. Hoeber, Inc., 1925, p. 89.

THE RELATION OF BROCA'S CENTER TO LEFTHANDEDNESS.

By Karl Rothschild, M.D.,

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(From the Department of Neuropsychiatry, St. Peter's General Hospital.)

The question of an intimate connection between righthandedness and the localization of speech has found ample consideration in the literature, varying from merely statistical observations to highly speculative considerations.

Recently 2 cases have come under my observation which present several very interesting features.

Case Reports. Case 1.—A young chemist came to my office complaining that the "stammering" from which he has been suffering for a number of years, has increased lately. On examination I find the heart slightly enlarged to the left and downward. Blood chemistry shows normal findings. Abdominal reflexes cannot be elicited. All tendon reflexes are more marked on the left than on the right side. The right pupil is slightly larger than the left, the right eyeground shows marked pigmentation in

its temporal half and the suspicion of a slightly choked disk. This patient has apparently, at one time or other, suffered an insult to his right hemisphere, possibly of an embolic nature. He is righthanded. Although suffering from an insult to his right hemisphere, his speech has become affected in the sense of paraphasia and paragraphia. When talking he omits syllables and especially endings of words. When writing he leaves out parts of words and again especially endings.

CASE 2.—I am at present treating a man suffering with postencephalitis, with a clinical picture typical for this disease. The tremors, however, are confined to his left hand. This peculiarity may be explained by the fact that he is lefthanded. Yet his parents as well as his brothers and sisters are all righthanded.

A few months ago his mother, who is righthanded, suffered an apoplectic insult, with paralysis of the left half of her body. At the same time she was unable to speak. In other words, a hemorrhage to the right side of the brain in this case caused aphasia.

In a recent study Riese[1] remarks that occasionally in the course of inheritance a complete righthander or lefthander may transmit to his children only "decidedness" of a certain brain territory and not of a whole hemisphere, which would give cause to incomplete "seitigkeitsanlagen" of the brain. He notes that an occasional person may be a righthander and yet may possess in the right hemisphere, which is generally considered inferior, certain superiorities, as, for instance, the control of speech.

Bethe[2] emphasizes that only a few individuals show a primary preference for the right hand and that the final preference for the right hand is due to exogenous influences. He finds that among younger children the percentage of distinctly righthanded or lefthanded individuals is the same for the two hands, while in a group of older children there are three times as many righthanders as there are lefthanders. These findings coincide with those by Kistler,[3] who, besides, finds that every fourth child and every eighth adult is lefthanded.

Bethe further concludes that righthandedness and the predominance of the left hemisphere stand in only loose and indirect connection. In his opinion there is no reason why the fact that the preference for one hand may develop the opposite hemisphere should be carried over to a combination of movements as bilateral as speech. He believes that the localization of the speech center on one side is more a congenital factor than is the case with other motor centers which may be affected by the practice of monolateral movements.

In Case 1, we may well assume that Broca's center is located in the right hemisphere. Yet this patient is righthanded and has always been so, no effort having been made on the part of his parents to correct this "abnormality." This is demonstrated by the fact that, while both parents are righthanded, 2 of their 8 children have always been lefthanders. Nobody else in the family shows any difficulty of speech. There is a definite probability that in

1 of the parents or at least in 1 of the antecedents Broca's center is also located in the right hemisphere. The case shows that in the course of inheritance characteristics of not a whole side of a brain, but of parts of one hemisphere, may be transmitted separately.

In Case 2, a son is the only lefthander in the whole family. But when his mother suffers an apoplectic insult to the right hemisphere her speech becomes affected. This means that in this woman righthandedness has been completely compatible with location of Broca's center in the right half of the cerebrum. Yet, in 1 child of hers the connection between speech center and preference for one side (for some reason thus far unexplained) has become so intrinsic that this child is lefthanded. Here again, we may assume that among the antecedents there were some with the "abnormality" of rightsided Broca's center and others with lefthandedness.

Statistical surveys show a primary ambidextry in spite of the prevalence of leftsided speech centers. Dextriposition may be more frequent than we generally assume. In 2 practical cases we have tried to show that this transposition bears no fundamental and intrinsic relation to the preference for the use of one or the other side of the body. It may, however, be that in some cases the location of the speech center on the right side is combined with a fundamental preponderance of the whole motor sphere of this side. Then we would have a case of clear leftsidedness from fundamental causes.

Summary. 1. Location of speech center and preference for one side of the body stand in only loose connection.

2. Location of Broca's center in the right hemisphere is compatible with righthandedness.

3. Description of 2 such cases, discovered following apoplectic insults, is herewith presented.

4. In both cases there are lefthanders and righthanders in the family. A combination of both "seitigkeitsanlagen" produces true leftsidedness.

REFERENCES.

1. Riese, W.: Zum Problem der Ueberwertigkeit der einen Hirnhälfte, München. med. Wchnschr., 1927, **74**, 1749.

2. Bethe, A.: Zur Statistik der Links-und Rechtshändigkeit und der Vorherrschaft einer Hemisphäre, Deutsch. med. Wchnschr., 1925, **51**, 681.

3. Kistler, K.: Linkshändigkeit und Sprachstörungen, Schweiz. med. Wchnschr., 1930, **60**, 32.

REVIEWS.

SURGERY: ITS PRINCIPLES AND PRACTICE. By ASTLEY PASTON COOPER ASHHURST, A.B., M.D., F.A.C.S. Professor of Clinical Surgery in the University of Pennsylvania. Pp. 1189; 1063 illustrations. Fourth edition thoroughly revised. Philadelphia: Lea & Febiger, 1931. Price, $10.00.

"So much that is of real interest has been added to our knowledge of surgery in the last couple of years, that instead of being able to reduce the total number of pages by thirty, as was done in the previous edition, it has now been necessary to increase the total number by five.

"Among the new matter introduced, or the sections which have been entirely rewritten or which have undergone more extensive revision than the rest of the book, may be mentioned giant-cell tumors; rectal and spinal anesthesia; contusions of bone; mycotic aneurysms, symmetrical gangrene, thrombo-angiitis obliterans, injection treatment of varicose veins; the osteochondritides, scoliosis, coxa vara; compression of the brain; the Bovie electrosurgical apparatus; hyperthyroidism; trans-illumination of the mammary gland; gastric and duodenal ulcers, cholelithiasis and gall-stone formation; and tumors of the sympathetic nervous system. There have been introduced in all 49 new illustrations (all original), of which 33 are replacements of former illustrations supplied as the opportunities arose to secure better materials; and 16 are entirely new, no originals of which were formerly available. There remain now scarcely any illustrations (except a few diagrams) in the book which are not original. . . .

"In the present work emphasis is placed on the underlying principles, and pathogenesis, diagnosis, and indications for treatment have received particular attention. Descriptions of operations, however, have not been slighted. The more important operations have been described in detail, and in every case an attempt has been made to present clearly, if briefly, at least one method of operative procedure. The specialties of the Eye, the Ear, the Nose, and the Throat naturally are not included; and Genito-urinary Surgery, Gynecology, and Orthopedics have been discussed only so far as they come within the province of the general surgeon."

(FROM AUTHOR'S PREFACE.)

THOMAS SAY. EARLY AMERICAN NATURALIST. By HARRY B. WEISS, and GRACE M. ZIEGLER. A Foreword by L. O. HOWARD. Pp. 260; illustrated. Springfield, Illinois: Charles C Thomas, 1931. Price, $5.00.

THOMAS SAY, "The Father of American Zoölogy," had several contacts with early American medicine. Descended from a Huguenot family long-resident in Pennsylvania, his father, Benjamin Say, studied drugs and medicine under the apprentice system then in vogue to become a successful physician-apothecary. He was prominent in several lines of civic activity and was chosen one of the Junior Fellows of the College of Physicians on its foundation in 1787, the year in which Thomas was born. Thomas himself was established by his father in the drug business in the firm of Speakman and Say, but their impractical habit fortunately soon produced failure, and allowed him to devote himself entirely to natural history.

A collecting trip to Florida and two others to the West, together with local expeditions in New Jersey and Pennsylvania, furnished material for many communications to the Academy of Natural Sciences and in 1824 for his pioneer book on American Entomology. Like his father, he had manifold interests. The Philosophical Society, the First City Troop on active service, Wistar Parties and such like afford the authors good opportunity for portraying early 19th century life in what was still the metropolis of the country.

The curious community experiment at New Harmony, Indiana, where Say spent his last decade until his death in 1834, and the evidence justifying the use of the opening term of this Review will be found in the later chapters composing the bulk of the book. Through the medium of a carefully portrayed individual life, a vivid picture of early American natural history and one of its chief pioneer, emerges. E. K.

LEONARDO DA VINCI. THE ANATOMIST. CARNEGIE INSTITUTION OF WASHINGTON, PUBLICATION NO. 411. By J. PLAYFAIR MCMURRICH, Professor of Anatomy and Dean of the School of Graduate Studies, University of Toronto, with a Preface by GEORGE SARTON. Pp. 262; 89 illustrations. Baltimore: The Williams & Wilkins Company, 1930. Price, $6.00.

BY many considered as one of the greatest men who ever lived, by all acknowledged to be one of the outstanding figures in an age prolific in geniuses, one of the very few to attain top rank in several fields of human endeavor, and yet with important phases of his life only recently unveiled or still shrouded in mystery, Leonardo presents a complex problem to a biographer. From the time that Dalton, the librarian of George III, burst the lock of the chest that

contained the precious manuscript buried for more than two centuries, the artist of the Last Supper and of the smile of Monna Lisa, the engineer and architect of the Milanese, the sculptor of the heroic bronze of Ludovico Sforza, the eminent botanist, zoölogist and agriculturist has awaited adequate treatment from the point of view of medical history. It was a fortunate suggestion of Dr. Sarton's, ten years ago, that secured for this purpose the services of "one in whom the technical and the historical, the scientific and the artistic qualifications" were so generously developed and nicely balanced.

While the author, himself an anatomist of note, attempts to evaluate only one of his subject's many activities, he has fortunately been led much further afield in his recognition of the need of a proper perspective for this survey. Though he presents his evidence in a dispassionate, analytic manner, the reader is forced to agree with the warmer words of Vasari, that Leonardo gave "veramente luce all'anatomia fino a quel tempo involta in molte e grandissime tenebre di ignoranza."

The numerous excellent reproductions of Leonardo's anatomical drawings, especially where the artistic touch was of major importance, conclusively show his ability, to observe accurately and independently. Some, however, and especially statements in his mirror-writing text, show his dependence on the Arabs even when it necessitates contradiction of the evidence of his own drawing. Thus we can agree with Sarton that, genius though he undoubtedly was, Leonardo belonged to his century as completely as many of his humbler contemporaries and that "This father of modern science was still in many respects a child of the Middle Ages."

E. K.

A System of Bacteriology in Relation to Medicine, Vol. 7, Virus Diseases, Bacteriophage. By various Authors. Pp. 509; illustrated. London: Medical Research Council, 1930. Obtainable in the United States at British Library of Information, 5 E. 45th St., New York. Price, £1/1/9 for this volume; for the set £8/14/9.

In the present volume of this great British System of Bacteriology is presented a thoroughly modern account of the important virus diseases and of the bacteriophage. The twenty-seven authors of the treatise are investigators of international reputation. The book begins with introductory chapters on viruses and virus diseases. The chapters following deal with individual virus diseases, such as smallpox, typhus, epidemic encephalitis, rabies, trachoma, warts, measles, leukemia of fowls, yellow fever, and so forth. The general treatment of the various diseases may be illustrated by citing the subjects discussed under lethargic encephalitis: history, sympto-

matology, pathology, comparative pathology, bacteriology, immunity, histology of experimental encephalitis in the rabbit, relationship of the virus of herpes febrilis to the etiology of encephalitis lethargica, summary, literature. The bibliography is excellent; the various authors have selected the more important contributions, and avoided unwieldly unnecessary repetition. The concluding chapter on bacteriophage and cognate phenomena is particularly noteworthy and represents a splendid review of our present-day knowledge. The entire work is thoroughly readable. Workers in the fields of pathology, bacteriology, immunology and the related sciences owe a debt of gratitude to the Medical Research Council of Great Britain under whose auspices the work has been prepared.

B. L.

SIR D'ARCY POWER. SELECTED WRITINGS 1877–1930. Anonymous. Pp. 368; illustrated. Oxford: Clarendon Press, 1931. Price, 25s. net.

A CHARMING series of 16 articles from the pen of an internationally prominent writer on surgery and medical history—given him by his friends on the occasion of his 75th birthday. It is only unfortunate that limitations of space prevented a fuller selection from the copious storehouse indicated in the 609 articles listed in his bibliography. The 26 illustrations are models to the medical publisher in their interest and freshness to the casual reader. While Harvey, John Hunter and St. Bartholomew's naturally occupy the foreground, the interesting topics range from English medicine in the fourteenth century to "Imaginary Annals of the Section of Comparative Medicine." We congratulate both the author and his editorial friends on this delightful volume.

E. K.

TREATMENT IN GENERAL PRACTICE. By HARRY BECKMAN, M.D., Professor of Pharmacology, Marquette University Medical School, Milwaukee, Wisconsin. Pp. 899. Philadelphia: W. B. Saunders Company, 1930. Price, $10.00.

"THE neglect of thorough and painstaking teaching of therapeutics in this country;" the presentation in most medical schools of "a riduculously inadequate course of lectures, usually to junior students who have had as yet practically no contact with the sick," the rest being left to the teachers in the department of medicine and the specialties who in the huge task of teaching the methodology of diagnosis have "no time left for an exhaustive consideration of the treatment of disease;" the consequent inadequacy of the average young practitioner's therapeutic knowledge: these are the author's reasons for writing this book.

There are described the treatments of the principal diseases of man, including most of those usually found in a textbook on medicine; also of certain genito-urinary affections; common diseases of the skin; burns; some obstetrical conditions. In each instance there is an introductory definition of the disease, and when indicated, a brief statement of the underlying pathology. In discussing treatment the author refers constantly to original sources (there are 32 pages of bibliography) with extensive quotations (there is 1 of 10 consecutive pages), well selected and with much good editorial comment by the author. One might quibble over some classifications: for example, malaria and sprue under "infections," or herpes zoster as a skin disease; and over some omissions (Banti's syndrome) and inclusions (ainhum). Few will share the author's enthusiasm for synthaline or will agree with his statement that enzymes will reappear in gastric achylia if enough acid is administered; or that allergy is really only a form of alkalosis (the Reviewer failed utterly to relieve hay fever patients by giving them nitrohydrochloric acid); or that the Christmas Seal educational campaign had little to do with the lowering of the death rate from tuberculosis (yet he admits elsewhere that "volume of organisms" is an important factor in determining the severity of all infections). We thought that most medical historians had exonerated Columbus' crew of the charge of introducing syphilis into Europe (Sudhoff, Karl: *Arch. de med., cir. y espec.*, 1929, **31**, 5). But after all, these are minor criticisms and the Reviewer hastens to counterbalance them by assuring practitioners that they will find in this book an exceedingly useful, convenient and interesting addition to their library. R. K.

THE METABOLISM OF TUMORS. Edited by OTTO WARBURG, Kaiser Wilhelm Institute for Biology, Berlin-Dahlem. Translated from the German edition, with accounts of additional recent researches by FRANK DICKENS, M.A., PH.D., Whole-time worker for the Medical Research Council at the Courtauld Institute of Biochemistry, Middlesex Hospital, London. Pp. 327; illustrated. New York: Richard R. Smith, Inc., 1931. Price, $12.00.

DURING the course of investigations upon the respiration of sea-urchin eggs Warburg observed that at the moment of fertilization oxygen utilization was tremendously increased. Attributing this increased oxygen uptake to a corresponding increase in the growth rate, he felt that application of the same method of study to other rapidly growing cells, namely, tumor cells, might show a similar magnitude of oxygen consumption. To his surprise he found that tumor cells, especially the cells of malignant tumors, consumed

comparatively little oxygen. A repetition of the experiment was made and to the special Ringer's solution in which the determinations were made, was added glucose. It was then observed that oxygen consumption was not increased. On the other hand the tumor tissue produced large quantities of lactic acid from the glucose, both in the presence and in the absence of oxygen. This was very different from the behavior of normal tissue, which produced very little if any lactic acid when oxygen was present, and much less than tumor tissue in the absence of oxygen.

These important observations were published in 1923. Before that time very little was known of the metabolism of the cancer cell or of its relation to normal body cells. In the interval many observations have been made and an entirely new mode of investigation into the nature of tumor growth has been developed.

The collected papers from Professor Warburg's laboratory were published first in German in 1926. The present volume in English will enable those interested in the cancer problem to follow through translations of the original papers the development of this work. The English edition has included several papers issued after the publication of the German edition, among these Professor Warburg's most recent paper (1929) in which he sets forth his theory as to the cause of tumor growth.

It is his opinion that if the ability of growing cells to use oxygen is injured in any way the cells that survive will be those that can derive their energy by glycolytic rather than by the ordinary oxidative processes. These cells, continuing to grow in this extraordinary way, will thus become tumor cells.

To those who may wish to use the Warburg technique for the study of cell metabolism it will be a great advantage to have the original directions, descriptions of apparatus and so forth in English.

E. W.

THE DEVELOPMENT OF PHYSIOLOGIC CHEMISTRY IN THE UNITED STATES. By RUSSELL H. CHITTENDEN, Professor of Physiological Chemistry in the Sheffield Scientific School of Yale University 1882–1922. Pp. 427. New York: The Chemical Catalog Company, Inc., 1930. Price, $4.50.

THIS valuable story of the development of biochemistry in this country, written by the dean of the American authorities on the subject, who has himself contributed much pioneer work in this field, shows "by explicit statements of actual experimental accomplishments, at different times and in different places, by many workers and groups of workers, something of the progress which has been made in this country during the past half century in the field of physiologic chemistry." It is one of a series of scientific and

technologic monographs published by the American Chemical Society, by arrangement with the Interallied Conference of Pure and Applied Chemistry, which met in London and Brussels in 1919.

No less truly historical than writings in other fields of biology that must perforce devote space to archaic ideas and methods, this book is able, while preserving the chronologic method of approach, to present a fair survey of the present status of biochemistry in many fields and a "suggestive outlook for the achievements of tomorrow." Where most of the contributions described have been by investigators who are living, the author has wisely abstained from critical analysis of the work or criticism, *pro* or *con*, of the workers.

Starting with the foundation of "the first physiologic laboratory for the use of students in the United States" by Bowditch at Harvard in the early seventies, the author, whose life study of the subject itself began in 1878, traces in the first 3 chapters the early general development of the subject in his country. The subsequent 9 chapters take up such topics as the study of proteins, the blood as a physico-chemical system, antiketogenesis, lipoids, anaphylaxis, oxidation reduction systems, vitamins, internal secretions, the chemistry of the brain and of the tubercle bacillus.

Consideration of the development of the specialty in such institutions as Columbia, the Universities of Pennsylvania and Michigan, the Mayo Foundation and a number of other institutions, permits inclusion of many valuable and interesting biographic details. With pardonable pride, the author brings out the important part played by the laboratory of physiologic chemistry at Yale, both as a center for research and in the number of students sent to important posts throughout the country.

We congratulate the American Chemical Society on this successful addition to American chemical literature "without primary regard to commercial considerations." E. K.

THROUGH THE ALIMENTARY CANAL WITH GUN AND CAMERA. Personally Conducted by GEORGE S. CHAPPELL. With an Introduction by ROBERT BENCHLEY. Pp. 231; 18 illustrations. New York: Frederick A. Stokes Company, 1930. Price, $2.00.

A BIT of humor now and then is relished by the wisest men and the author, friend of the gallant Traprock and the famous square egged fatuliva bird, furnishes plenty in this venturesome journey through the "abominable regions." As Robert Benchley says, the "book ought to cause quite a stir in digestive circles." Among the illustrations, I prefer "My Castle on the River Bile."

E. K.

BOOKS RECEIVED.

NEW BOOKS.

International Studies. Prevention and Treatment of Disease. Conducted for The Milbank Memorial Fund by SIR ARTHUR NEWSHOLME, K.C.B., M.D., F.R.C.P. *Vol. I. The Netherlands, Scandinavia, Germany, Austria, Switzerland.* Pp. 248. Baltimore: The Williams & Wilkins Company, 1931.

Text Book of Physical Therapy, Vol. I. By WILLIAM BENHAM SNOW. Pp. 708; 183 illustrations. New York: Scientific Authors' Publishing Company, 1931. Price, $10.00.

Harper's Medical Monographs. Vols. I and II. Treatment of Injury. By CLAY RAY MURRAY, M.D., F.A.C.S., Assistant Professor of Surgery, College of Physicians and Surgeons, Columbia University. Pp. 412; 196 illustrations. New York: Harper & Brothers, 1931. Price, 2 vols., $5.00.

Chemistry for Nurses. By HARRY C. BIDDLE, A.M., Instructor in Chemistry, School of Nursing, Western Reserve University. Pp. 336; 74 illustrations. Philadelphia: F. A. Davis Company, 1931. Price, $2.75.

Collected Reprints from the Laboratories of the Mount Sinai Hospital, New York, 1930.

Medizinische Praxis. Band XII. Herz- und Kreislauf-Insuffizienz. By DR. K. F. WENCKEBACH, Em. Vorstand der I. Medizinischen Universitatsklinik, Wien. Pp. 120; 7 illustrations. Leipzig: Theodor Steinkopff, 1931. Price, gehefted RM 8.00, gebunden RM 9.50.

Peptic Ulcer. A Symposium of the Current Literature. Pp. 78; 8 illustrations. New Haven: The BiSoDol Company, 1931.

The Renal Lesion in Bright's Disease. By THOMAS ADDIS, Professor of Medicine, Stanford University, and JEAN OLIVER, Professor of Pathology, Long Island College of Medicine, formerly Professor of Pathology, Stanford University. Pp. 628; 170 full-page plates, 2 in color; 21 illustrations and 1 folding table. New York: Paul B. Hoeber, Inc., 1931. Price, $16.00.

The International Medical Annual. Forty-ninth Year, 1931. Pp. 551; 53 illustrations, 70 plates. New York: William Wood & Co. 1931. Price, $6.00.

The Surgical Clinics of North America. Vol. II, No. 2 (Lahey Clinic Number, April, 1931). Pp. 248; 88 illustrations. Philadelphia: W. B. Saunders Company, 1931.

Trabajos y Publicaciones de la Clinica del Professor Pedo Escudero, Vol. Cuarto, 1930. Buenos Aires: Pedro Garcia, 1930.

Geneeskundige Kunstkalender Voor Heb Jaar 1931. 25 illustrations. The Hague: J. Philip Kruseman. Price, $1.50.

Noguchi. By GUS ECKSTEIN. Pp. 419; illustrated. New York: Harper & Brothers, 1931. Price, $5.00.

Rembrandt. By DR. J. G. DE LINT. Pp. 113; 64 illustrations. The Hague: J. Philip Kruseman, 1931. Price, $2.50.

The Treatment of Asthma. By A. H. DOUTHWAITE, M.D., F.R.C.P. (LOND.), Assistant Physician, Guy's Hospital. Pp. 164; New York: William Wood & Co., 1931. Price, $2.50.

On the Principle of Renal Function. By GOSTA EKEHORN, M.L. Pp. 717; 60 illustrations. Stockholm: P. A. Norstedt & Soner, 1931.

A Manual of Practical Vertebrate Morphology. By J. T. SAUNDERS and S. M. MANTON. Pp. 220; 43 illustrations. New York: Oxford University Press, 1931. Price, $5.00.

NEW EDITIONS.

Nutrition and Diet in Health and Disease. By JAMES S. MCLESTER, M.D., Professor of Medicine at the University of Alabama, Birmingham. Pp. 891. Second edition, revised and reset. Philadelphia: W. B. Saunders Company, 1931. Price, $8.50.

The rapid recent advances in the science of nutrition have necessitated many changes since the first edition of this book. (See AM. J. MED. SCI., 1927, **176**, 436.) Vitamins, diabetes, obesity, digestive disorders and even gout thus have required considerable modification and additions. Sections have been added on toxemias of pregnancy, colon and protozoan infections.

Diagnostic Methods and Interpretations in Internal Medicine. By SAMUEL A. LOEWENBURG, M.D., F.A.C.P., Associate Professor of Medicine, Jefferson Medical College. Pp. 1032; 547 illustrations. Second revised edition. Philadelphia: F. A. Davis Company, 1931. Price, $10.00.

Fundamentals of Dermatology. By ALFRED SCHALEK, M.D., Professor of Dermatology and Syphilology, University of Nebraska College of Medicine. Pp. 247; 58 illustrations. Second edition thoroughly revised. Philadelphia: Lea & Febiger, 1931. Price, $3.00.

Thoroughly revised and considerably enlarged, it covers the anatomy, physiology, symptomatology, diagnosis, prognosis and treatment of skin diseases in reasonably good manner in the limited space available.

Clinical Diagnosis by Laboratory Methods. By JAMES CAMPBELL TODD, PH.B., M.D., late Professor of Clinical Pathology, University of Colorado School of Medicine, and ARTHUR HAWLEY SANFORD, A.M., M.D., Professor of Clinical Pathology, University of Minnesota (The Mayo Foundation), Head of Section on Clinical Laboratories, Mayo Clinic. Pp. 765; 347 illustrations, 29 in colors. Seventh edition, thoroughly revised. Philadelphia: W. B. Saunders Company, 1931. Price, $6.00.

This excellent manual, one of the best of its kind, should need no further introduction to medical readers. Dr. Sanford has upheld the high standard of previous editions. New methods for the culture of tubercle bacilli, determination of lead, precipitation of proteins from body fluids, blood sugar and uric acid, calcium, blood volume, use of histamin in gastric analyses, occult blood, Ascheim-Zondek test and others are included.

Clinical Electrocardiography. By SIR THOMAS LEWIS, M.D., F.R.S., D.Sc., LL.D., F.R.C.P., C.B.E., Physician of the Staff of the Medical Research Council; Physician in Charge of Department of Clinical Research, University College Hospital. Pp. 128; 107 illustrations. Fifth edition. London: Shaw & Sons, Ltd., 1931. Price, 8s 6d.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF
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The Relationship of Blood Uric Acid Content to the State of Renal Function in Nephritis.—The blood urea clearance test has been found to be an extremely satisfactory method of estimating renal function (Moller, McIntosh and Van Slyke. The only difficulty with this method is that it is a trifle too complicated to be carried out as a common clinical procedure. However, as a method of comparing other renal function tests and determining their value and their worth in the laboratory, it is a procedure which seems to be the most accurate of any method used. The determination of uric acid concentration in the blood, with a simultaneous estimation of nonprotein nitrogen and creatinine, is a method which is very generally employed more or less routinely, often under the broad term of "blood chemistry." Medical men everywhere have the idea that the estimation of the waste products of nitrogenous metabolism in the circulating blood offers a practical method of determining the function of the kidney at any given time. High concentration of the uric acid is presumably definitely due to renal pathology. CHRISTOPHER JOHNSTON (*J. Clin. Invest.*, 1931, **9**, 555) compares the urea clearance test with the concentration of uric acid in the blood. One hundred and seventeen tests were made on 30 patients, 21 of whom had chronic nephritis of the hemorrhagic type, 2 of whom had the acute hemorrhagic type of nephritis, 3 chronic degenerative, 3 arteriosclerotic, and the tests of 1 patient were carried out when he was in a condition of cardiac failure. The data that Johnston collected show that normal figures for blood uric acid occur in a very large number of nephritic cases, even with the urea excreting power being only 20 per cent of normal. Moderately increased blood

uric acid may be present when there is only slight renal damage or the most extreme loss of function. High blood uric acid figures occur only when the nephritis has attained an advanced degree, with the urea excreting power less than one-fifth of normal. This irregular correlation of blood uric acid to renal function, the author says, was to be anticipated, as uric acid is removed from the organism in part only by excretion. He concludes that the determination of blood uric acid as an indicator of renal function is of little value.

The Excretion of Intravenously Injected Bilirubin as a Test of Liver Function.—HARROP, and GUZMAN BARRON (*J. Clin. Invest.*, 1931, **9**, 577) write that the liver plays such an important rôle in the normal body that numerous methods have been advanced for the study of the functional efficiency of this organ. It has, however, more than one function and it is quite conceivable that dissociated functional disturbances may arise when the gland is acted upon by any noxious substance. Some of the functions are possibly more susceptible to the action of these injurious agents than others and among these there appears to be the inability of the liver to excrete bilirubin despite the fact that other functions of the liver are still unimpaired. The Van den Bergh reaction has been extensively employed to determine the degree of injury to the liver cells. It is assumed, however, that this particular reaction depends very largely upon extensive liver injury, as the factor of safety of this particular organ is very great. Certainly there exist many conditions of mild liver injury where bilirubinemia is not increased. The authors have made the basis of their study the concept that if an increased amount of bilirubin is injected into animal or man, insufficiency of liver may be demonstrated; assuming, as they bring out in their article, that evidence seems to indicate definitely that bilirubin is excreted *in toto* by the liver, that it is not retained by the cells of the reticulo-endothelial system, and that it is not excreted by the kidneys. They employed for their examinations bilirubin injections in dosage of 1 mg. per kilo of body weight in an alkaline solution, and the bilirubin of the blood was determined by the method of Ernst and Förster. They found in the normal individual the amount of bilirubin given above is excreted in from two to four hours, and in the majority of instances in three hours after the injection. Four hours they consider the maximum limit of the total excretion in normal individuals. The series of patients they studied were those in whom it was presumed that there was some slight disturbance of liver function, such as Rich and Resnik have observed in pernicious anemia and experimentally produced anemias. In this particular series of cases of anemia there was a definite retention of bilirubin at the end of four hours. In the second series, the patients were suffering from a variety of pathologic conditions, such as cirrhosis of the liver, postarsphenamin jaundice some months after clinical recovery, typhoid fever, and acute infectious diseases. It was found again in these diseases that there was a retention of this particular pigment. As a result of the study of this series of cases, the authors feel they are justified in concluding that "the bilirubin excretory power of the liver is the most delicate method so far proposed for testing the functional capacity of this organ."

SURGERY

UNDER THE CHARGE OF
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Peritonitis.—Meloney, Harvey and Jern (*Arch. Surg.*, 1931, **22**, 1) state that it cannot be too strongly emphasized that the most important prophylactic treatment for peritonitis, as seen in a general surgical hospital, is early diagnosis and early operation in acute appendicitis. A comparison of smear and culture with the pathologic condition at the time of operation gives a sound basis for prognosis. In the great majority of cases yielding bacteria in their series, there was a polymicrobic infection. In any specific prophylactic or active treatment for bacterial peritonitis, one must take into consideration the symbiosis of the commonest organisms found in the peritoneal exudate, namely, Bacillus coli and Bacillus welchii. The mortality in perforative cases was so much greater than in the nonperforative cases in their series that the rôle of the intestinal juices must not be forgotten. The results of this study lay the ground work and point the way to some specific experimental studies, of which may be mentioned: (*a*) vaccine and serum prophylactic and active treatment; (*b*) the bacteriostatic effect of peritoneal fluids; (*c*) the neutralization of digestive ferments, and (*d*) the synergisms and antagonisms of certain bacteria.

The Intervertebral Disks.—Smith (*Brit. J. Surg.*, 1931, **18**, 385), says that the objects of the research, the results of which are given in this paper were to verify certain debatable points about the structure of the intervertebral disks and to determine the mode of nutrition, the state of the disks from infancy to old age and the diseases to which they are subject. The intervertebral disks are rudimentary diarthrodial joints possessing a cavity filled with villi, a fibrocartilaginous capsule, and upper and lower cartilaginous plates comparable to articular cartilages. The mode of nutrition is by blood channels, which pierce the cartilaginous plates from the marrow of the vertebral bodies. The disks allow a small degree of movement in all directions between the vertebræ and thus are highly important in imparting flexibility to the spine. They are also powerful buffers between the vertebræ, absorbing shocks transmitted along the spine. In the first two decades of life, an intervertebral disk is biconvex and highly elastic. The fibers of the annulus are fine and white, the cartilaginous plates thin, translucent and bluish white. In subsequent decades the disk tends to become progressively more coarse, inelastic, tough and discolored. The lesions of the disks which have up until now been described are fibrous, cartilaginous, calcareous, bony fatty, necrotic and liquefactive changes. Inflammatory changes are thought to be secondary to an affection of the spongiosa of the corpus vertebræ. In osteochondritis of the spine, the disks are affected as well as the vertebræ. There seems to be some reciprocal adaptability between the disks and the vertebræ

when either are diseased. Diagnosis of the lesions of the intervertebral disks depends on radiographic examination. Thinning and flattening, diminished transparency, peripheral or central calcification, obliteration by ossification or abnormal biconvexity, may be observed.

Transplantation of Ureters to the Sigmoid. — SISK, WEAR and O'BRIEN (*Surg., Gynec. and Obst.*, 1931, **52**, 212) claim that the transplantation of the ureters to the sigmoid in dogs is highly unsatisfactory by the Mayo technique. In every case the kidney became infected and closure of the uretero-sigmoidal opening by the mucosa of the bowel occurred in 5 of the 7 unilateral transplants. In the 2 bilateral transplants the ureteral openings were markedly stenosed. The completed Coffey technique gave slightly better results. Of the 8 dogs 4 showed bilateral infection, 3 showed infection on only one side and 1 showed no evidence of infection, but was hydronephrotic on one side. Complete closure of the ureteral opening occurred in only one ureter. The unilateral Coffey operations revealed kidneys in which there was no microscopic evidence of pyogenic infection, yet the dogs never appeared well after operation. Believing that the kidneys became infected by means other than the lumen of the ureter, the authors obtained infected kidneys in 2 cases in which the ureters were still completely obstructed at autopsy. The lymphatics must be given serious consideration as a means of transmitting infection to the kidneys. Solution of the problem of preventing ascending renal infection probably depends upon the discovery of means to prevent infection through the lymphatics. Partial success in this direction was obtained in experiments in which the authors tried to protect the exposed end of the ureter for a time from infected material. Until a uniformly successful procedure is evolved, it would seem the better surgical judgment to use ureteral transplant only in those cases in which older and better understood methods are impossible.

Experiences With the Cerebellar Astrocytomas.—CUSHING (*Surg., Gynec. and Obst.*, 1931, **52**, 129) says that the cerebellar astrocytomas furnish another example of gliomatous tumors which show predilection for a favorite site and produce a recognizable syndrome. The tumors are probably of congenital origin and usually date symptomatically from childhood, the average age on admission being thirteen years. They are signalized by period matutinal headache and vomiting owing to their midcerebellar situation, the tumors invarably cause secondary hydrocephalus and this in turn leads to a choked disk, which may be so insidious in origin that seriously impaired vision may be the first recorded symptom. They may attain a surprisingly large size before any cerebellar signs, usually shown as instability, put in an appearance. The clinical diagnosis lies between astrocytoma and other forms of tumor that frequent the same region, medulloblastoma, angioblastoma and ependymoma, of which the astrocytomata are the most numerous. The tumors may lie exposed on the surface, or be wholly concealed, and when so concealed a vertical invasion through the vermis is the proper method of bringing them into view.

THERAPEUTICS

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Congo-red as a Hemostypticum.—WEDERKIND, BECKER and WIENERT (*München. med. Wchnschr.*, 1930, p. 2049) injected intravenously 5 to 10 cc. of sterile 1 per cent solution of Congo-red in cases with bleeding. The result of this therapeutic measure in 19 cases in whom the bleeding was caused by pulmonary tuberculosis, bronchiectasis, menorrhagia, tooth extraction, duodenal ulcers and malignancy is reported. The authors claim that the bleeding stopped between one-half to six hours following the intravenous injection of the Congo-red; and present some evidence that Congo-red stimulates the reticulo-endothelial system, increases the blood platelets and the fibrinogen content of the blood.

Convalescent Serum in the Prophylactic Treatment of Measles.—Serum or whole blood obtained from patients recovering from infectious diseases has repeatedly been used therapeutically. NABARRO and SIGNY (*Brit. Med. J.*, 1931, vol. **12**) state that at present human convalescent serum is far more reliable than the available animal serum. The serum is obtained from adults suffering from measles. Each patient is carefully examined before bleeding and particular notice taken of any syphilitic or tuberculous taint. Between the seventh and the fourteenth days after defervescence, 200 to 300 cc. of blood are collected asceptically into sterile oxalate solution. The serum is separated after the oxalate is precipitated with calcium chlorid. If the sterility test and the Wassermann reaction are satisfactory, 0.5 per cent phenol is added and the serum then pooled with other sera so as to obtain a product of uniform potency. In order to achieve complete protection, the serum should be injected before the fifth or sixth day of incubation. This results in a passive immunity which lasts roughly a month. If injected from the sixth to the ninth day, the serum does not protect fully and a very mild attack of measles may ensue. No benefit can be expected from injection after the ninth day. The mild attack which follows the late administration of serum manifests itself in a temperature of 100° F., which appears about the fourteenth day of the incubation and lasts for a day or two. A few measly spots over the trunk and mild coryza may appear for a day or two. Koplik's spots are never observed. A disturbing aspect is the prolongation of the incubation period, which may last for twenty-six days. The

satisfactory dose is 5 to 7 cc. given intramuscularly into the buttock. The serum has no value in the treatment of severe cases of measles. In a series of 586 cases, of which 461 were hospital cases and 125 from private practice, failure was observed in 3 per cent and 5.6 per cent of the cases respectively, to whom prophylactic treatment was given. Several of the cases in which the treatment failed were injected after the fifth day.

Experiences With Symbiotic Serum in Diphtheria.—Following the observations of Canon and Haaken on the frequency with which diphtheria was found to be combined with streptococcal infection, MEDEM (*Deutsch. med. Wchnschr.*, 1931, **57**, 146) employed a stock polyvalent streptococcic serum in combination with diphtheria antitoxin in the treatment of a group of cases, but saw no significant benefit. By cultures from the membranes and from puncture of the inflamed cervical nodes, he was able to find, however, streptococci in at least 50 per cent of all cases. Believing that these streptococci were somewhat modified by their symbiosis with the diphtheria bacilli, he then begen to employ a mixed serum prepared from cultures obtained from patients suffering from diphtheria. This combined or symbiotic serum represents an unconcentrated diphtheria antitoxin plus a streptococcus antiserum. Used in 50 cases of septic diphtheria, the results were most gratifying, only 2 of the 50 failing to recover, both of which were severely intoxicated and first seen on the fifth and sixth days respectively of their disease. Medem feels that it is too soon to speak positively as to the value of this symbiotic serum. He feels definitely that it has considerable promise of improving the treatment of diphtheria in its septic forms.

A Remarkably Active Liver Extract Which Produces a Beneficial Response in Pernicious Anemia and in Combined System Disease.—In a previous abstract published in this column attention was called to Gänsslen's preparation of a liver extract which when injected intravenously in amounts of 1 to 2 cc. daily, corresponding to 5 to 10 gm. of fresh liver, resulted in a remission within ten to fifteen days in patients with pernicious anemia. SCHILLING (*Klin. Wchnschr.*, 1931, **10**, 301) now confirms Gänsslen's claims and reports his experiences with special reference to the problems of "liver resistance" and combined system disease. The discussion centers on those patients with pernicious anemia in whom every other therapeutic measure failed after proper application, and additionally on a group of patients to whom, for various reasons, liver could not be administered successfully by mouth. Comparing his results with those from other extracts, Schilling affirms that Gänsslen's extract is not only a potent preparation but distinctly better than any other preparation in use. The efficacy of this extract is also shown by the fact that it produces a remission even in cases with such complications, in which other liver extracts failed. Schilling believes that the failure of orally administered extracts may be due to faulty absorption through the gastro-intestinal canal. He observes that patients with combined system disease show improvement following the injection of the Gänsslen extract. The degree of improvement is

similar to that observed after the oral administration of large amounts of raw liver in cases in which oral administration of liver extracts did not seem to benefit the patients. Schilling also observed considerable improvement in the general condition of his patients. The appearance and the turgor of the tissues improved. There was an increase in the capacity for work. It is noteworthy that improvement in the general condition of the patient was observed even in cases in which the blood findings had been brought to normal by liver therapy but with no improvement in the general condition. Such observations were made especially on elderly patients who continued to complain of paresthesias, mental depressions and lack of appetite, although their hemoglobin reached such high values as 90 to 100 per cent following daily doses of 250 gm. of liver. Schilling considers the Gänsslen extract a distinct advance in the liver therapy of pernicious anemia.

PEDIATRICS

UNDER THE CHARGE OF
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The Prevention of Rickets in Premature Infants by the Use of Viosterol 100-D.—May (*J. Am. Med. Assn.*, 1931, **96**, 1376) instituted this study in order to determine the dosage of viosterol for the prevention of rickets in premature children. It was soon apparent that there was a definite improvement in the weight, general well-being, hemoglobin concentration, calcium-phosphorus index and bone development in those infants constantly under supervision who received an adequate dose of viosterol, in contrast with those infants whose mothers were somewhat indifferent about following instructions as to the daily administration of viosterol, and the general care and feeding of the infant. Nearly every newborn infant is endowed with the amount of calcium and phosphorus in its body necessary to maintain a satisfactory balance until such time as adequate amounts are received through the mother's milk. This is especially true of the full-term infant. The artificially-fed baby may do well for many weeks without requiring an extra supply of vitamin D to keep up a normal calcium and phosphorus balance. On the other hand, the premature baby may be more susceptible to the development of a negative calcium-phosphorus balance on account of difficulty in ingesting enough milk, even by gavage, during the first few weeks of life. It is an accepted fact that premature infants are prone to develop rickets. They possess other physical inadequacies which directly or indirectly cause a high death rate in the first weeks of life. In respect to the high incidence of rickets, it does not seem to be entirely due to the inability of the infant to take sufficient milk, nor has it been established that a depletion of calcium and phosphorus necessarily occurs when the milk intake is subnormal. The relation of

intrinsic and available extrinsic calcium and phosphorus to their utilization after adequate administration of vitamin D is not well understood, and, until this biologic phenomenon is fully explained, exact procedures for the prevention of rickets cannot be planned. It is increasingly apparent that vitamin D in the form of viosterol is a vitally important factor early in life of those infants highly susceptible to rickets, and its judicious use from the first day of birth seems to increase the possibility of their survival and normal growth.

Chronic Stridor in Childhood, Sometimes Erroneously Attributed to Enlargement of the Thymus.—KENNEDY and NEW (*J. Am. Med. Assn.* 1931, **96**, 1286) says that the diagnosis of enlarged thymus is frequently made in cases in which further examination has disclosed other conditions as the cause of symptoms. Stridor, dyspnea, hoarseness, spells cyanosis and wheezy and noisy respiration can usually be accounted for on other bases than enlarged thymus. Laryngoscopic examination is often essential for definite diagnosis. Enlargement of the thymus can seldom, if ever, be established as a cause of death. Pre-operative examination and care of infants and children should be directed toward finding and correcting all conditions affecting surgical risk. Unjustified reports have caused the assumption that enlargement of the thymus accounts for much morbidity and mortality in infancy and childhood. The authors have not found it necessary to carry out pre-operative Roentgen therapy. They do give, however, a great deal of attention and pre-operative care to those children showing evidence of infection of the upper respiratory tract, fever, anemia, cardiac and renal disease, malnutrition, gastrointestinal disease and other conditions which might increase the operative risk.

On Enuresis.—MANDEL (*Brit. J. Child. Dis.*, 1931, **28**, 1) classifies the types of enuresis so as to make them clinically more easily recognized, and with a view of choosing the approved method of treatment which should be adopted. First there are those in which there is some physical irritant, such as worms, overdistention of the bladder, cystitis and the like. The hypersensitive, neuropathic or nervous type shows instability as the symptom which may be regarded as of importance equally with such symptoms as cyclic vomiting, ketonuria, vagotonia and the like. These respond to dietetic and medicinal treatment combined with readjustment of environment and reëducation. The so-called psychopathic child, in whom the enuresis is more a behavior complex, requires treatment directed toward the psychologic aspect. In endocrine dysharmony, particularly hypothyroidism, there develops a loss of inhibition. Small doses of thyroid give results, especially if aided by the use of pituitrin for its tonic effect on unstriped muscle. A final cause is seen in the debilitated child. In such general tonic treatment gives results. In all cases atropin or belladonna is the specific drug.

A Syndrome Characterized by Congenital Clouding of the Cornea.—HELMHOLTZ and HARRINGTON (*Am. J. Dis. Child.*, 1931, **41**, 793) found that there were many references in the literature on cloudy swelling of the cornea, but that few definite cases are reported, and that most

of the discussion is in regards to the cause of the condition, about which there are different opinions. Some writers are convinced that the corneal lesion is noninflammatory, owing either to arrested development in early uterine life, which results in failure of the cornea to become transparent, or to a nutritional disturbance of some kind. Others are equally insistent that the lesion is due to intrauterine inflammation, and that it is secondary to inflammation of the entire uveal tract. They base their claims on pathologic examinations, and consider syphilis as the most common etiologic factor. It is rather difficult, however, to accept this, as syphilis is common and corneal clouding is rare, and also because of the absence of other syphilitic manifestations in these cases. Many cases of corneal clouding have cleared up within a few months after birth. In such cases it is believed that the condition is due to redundancy of aqueous humor rather than to arrested development. In the cases reported by the author there was no evidence of syphilis and no history to suggest early inflammation. They do not have an adequate explanation of the etiology. The most striking feature is the uniform cloudiness of the cornea. This along with other anomalies, places the condition in a special group, forming a clinical syndrome. The characteristic of the syndrome are the uniform cloudiness of the cornea; short, thick, clawlike hands and feet, with limited extension; restricted motion of the joints of the extremities; lumbar kyphosis; scaphocephalic head and mental retardation.

Acute Encephalitis During Childhood.—HOLZMANN (*Deutsch. med. Wchnschr.*, 1931, **57**, 144) states that because of the many clinical manifestations, the differential diagnosis of encephalitis is extremely difficult. Two cases of encephalitis in children are described. In a girl, aged 7 years, the clinical picture suggested a meningitis of tuberculous character. The spinal puncture did not corroborate this diagnosis, because the pressure was not abnormally high, the albumin reaction was negative and the cellular elements were not increased. It was found that the sugar content of the cerebrospinal fluid was extremely high, being 285 mg. per 100 cc. The normal sugar content of the cerebrospinal fluid ranges from 50 to 75 mg. per 100 cc., and in tuberculous meningitis the sugar content may even be lower. Several investigators have observed an increased sugar content in cases of encephalitis. This case was for that reason diagnosed as encephalitis. Clinical symptoms which suggested encephalitis rather than meningitis were the accelerated pulse and the leukocytosis. The patient recovered completely, and with no nervous stigmata. The second patient was a boy, aged 3 years, who showed the symptoms of a hyperkinetic form of encephalitis. In this case also the spinal fluid was shown to contain excessive amounts of sugar but was free from albumin and showed no increase in the cellular elements. This patient died, but no necropsy was performed. The author feels that the increased sugar concentration of the cerebrospinal fluid is a valuable point in the differential diagnosis. That a high sugar concentration indicates an unfavorable prognosis was not corroborated by these observations. It seems that the sugar content is especially high in cases in which the respiratory disturbances are present. This is seen where inflammation of the medulla oblongata is especially pronounced.

DERMATOLOGY AND SYPHILIS

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Comparative Excretion and Absorption of Different Bismuth Products.—HANZLIK and MEHRTENS (*Arch. Derm. and Syph.*, 1930, **22**, 861), summarize their exhaustive studies on the clinical excretion of bismuth reported by the authors in the same and the two preceding numbers of the Archives of Dermatology, and in addition include a table of bismuth products with average bismuth content and a brief comparative résumé of absorptive studies in animals. The bismuth content in the products examined ranged from 20 to 75 per cent, but the authors believe that this factor is less important in the choice of a product than the criteria of vehicle, solubility, tolerance, absorption, and excretion. The adjustment of dosage can be made to compensate for variations in bismuth content. The following are a few of the more important conclusions: (1) A comparison of the clinical urinary excretion of bismuth during the first two weeks after the intramuscular injection of the different types of bismuth indicates that the water-soluble bismuth sodium tartrate, used in aqueous medium, was more efficiently absorbed than the insoluble products, used in oil or in aqueous medium (bismuth metal, potassium bismuth tartrate, and bismuth salicylate). (2) In general, increasing the dosage of bismuth products tends to diminish the total urinary excretion independent of the time factor and regardless of the bismuth product and the vehicle used. The cause of this is not understood, but certain possibilities are discussed. The phenomenon indicates the accumulation of bismuth in the body with increasing dosage. It is suggested that intensive medication and the use of total doses the equivalent of from 1 to 2.4 gm. of bismuth should be avoided. (3) The desirability of using small repeated doses instead of intensive medication for maintaining a uniform saturation of the tissues in the treatment for syphilis is suggested. (4) Generally, the results given in the literature indicate that the clinical use of different bismuth products in similar, equivalent doses of bismuth in lower therapeutic ranges (about 0.3 gm.) appear to give a similar total urinary excretion of bismuth, regardless of the bismuth product and the vehicle used. (5) The comparative total excretion of bismuth after the intramuscular injection of different bismuth products in different animals, as reported in the literature, is generally smaller than the clinical excretion, due apparently to the use of higher doses of bismuth; doses within the toxic fatal range showed smaller excretions than did those within the thera-

peutic range. Exact comparison of the different products was impossible on account of several variables affecting the results. (6) Collectively, the results given in the literature on the absorption of bismuth, obtained by the chemical analysis of tissues after the injection of different products of bismuth, indicate that all types of bismuth are well absorbed from the site of injection, regardless of the type or vehicle; the poorest absorption occurred with the insoluble products, used in oil or aqueous medium, and the greatest with soluble products, used in aqueous medium. Compared with the results on total excretion in animals, those on absorption showed an apparent lack of correlation; that is, much more bismuth would seem to be retained in the body according to the excretory results than according to those on absorption. After urinary excretion is completed, roughly one-half of the administered bismuth remains in the body to be gradually excreted over long periods in amounts too small to be detected. (7) The comparative fecal excretion of different bismuth products is similar and too small to account for the bismuth unaccounted for in urine. The median fecal excretion is about one-eighth of that in urine, indicating that the main channel of excretion is the kidney, which correlates with a high selective distribution of bismuth to this organ. (8) From considerations of clinical and animal results on excretion and absorption, and providing everything else is satisfactory, the choice of cationic bismuth products would appear to favor the water-soluble type, used in aqueous or tissue-soluble medium; this insures prompt and efficient tissue distribution and saturation, with corresponding antisyphilitic efficiency. Insoluble products of bismuth and insoluble vehicles are objectionable for well-known reasons, although the absorption and excretion of bismuth may be as good as after the administration of soluble products. Improvements on the soluble bismuth products are desirable as regards the vehicle for administration (this may be achieved by the use of ethylene glycol), and as regards the choice of products for efficient penetration of the brain, those containing bismuth as anion appear promising.

Experimental Studies in Eczema.—KLAUDER and BROWN (*Arch. Derm. and Syph.*, 1930, **22**, 877), have studied the potassium, total and diffusible calcium ratios in the blood of 107 patients with 24 different diseases of the skin as a further elaboration of their animal experimental work showing that the ratio of calcium and potassium ions largely governs the degree of irritability of the skin. The authors preface their study with a summary of the work done on serum calcium in patients with dermatoses and review in detail the accepted functions of calcium in the body. They stress the point that an estimation of total serum calcium is no index of available calcium for it has been shown that only 50 to 70 per cent of blood calcium is in diffusible form, and that of this amount but 15 to 25 per cent is ionized. The authors selected for study those diseases of the skin in which the sympathetic nervous system is apparently concerned in the pathogenesis (that is, generalized pruritus, urticaria, angioneurotic edema, prurigo of Besnier), and calculated the percentage diffusible calcium of total calcium, the potassium-calcium ratio and the potassium-diffusible calcium ratio. The latter two ratios

were then correlated one with another and compared with the ratios obtained in normal persons and patients with other dermatoses. The following figures were regarded as normal: total serum calcium, 9 to 11; total serum potassium, 18 to 20; percentage of diffusible calcium of total calcium, from 45 to 55 per cent; potassium-calcium ratio up to 2.10; potassium-diffusible calcium ratio, from 3.50 to 4.50. The data presented show that the calcium and potassium range in patients with different dermatoses was generally normal. The abnormal ratios were rarely striking in character and were not constant in all cases of the disease under investigation. The prurigo of Besnier (diathetic eczema) gave the most abnormal ratios due to the greater decrease of diffusible calcium. In this condition 5 of 9 patients had an abnormally high potassium-calcium ratio and 7 of the 9 had abnormally high potassium-diffusible calcium ratios (below 4.50). Besnier's prurigo is a member of the asthma-eczema-hayfever group of allergic diseases and the authors believe is associated with abnormal functioning of the vegetative nervous system and endocrine dysfunction, especially hypoadrenia. A table is included showing the change from abnormally high ratios to normal ratios after the administration of sympathetico-tonic drugs (calcium, epinephrin, atropin, ultraviolet, codliver oil, diet), and the authors conclude that this type of therapy is indicated in some but not all patients with pruritus accompanied with neurosis, urticaria, dermatographism, and especially the prurigo of Besnier.

GYNECOLOGY AND OBSTETRICS

UNDER THE CHARGE OF

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Myomectomy.—For 18 years BONNEY (*Lancet*, 1931, **220**, 171) has been extending the possibilities of myomectomy, until now he feels that it is unusual to meet a case of fibroids, no matter how numerous the tumors, how large or how placed, that is beyond the scope of conservative surgery. During this period of his intensive work he has performed the operation 403 times. The tumors were solitary in 166 cases and multiple in 237 cases. The greatest number of fibroids he has removed from a single uterus is 125, and after this 92, 80, 55, 52, 48, 46 and 44, while on 28 occasions the number has varied between 15 and 30. Just as the number of tumors is no bar to the operation, neither is the size of the growth, as he has performed the operation where the total mass was about that of a full-term pregnancy. He emphasizes that the ease

or the difficulty of the operation depends less on the size and the number of tumors than on the position they occupy in the uterus. Thus a tumor on the lateral wall is more troublesome to remove than one on the anterior wall and a tumor in the posterior wall more difficult than either. There have been 7 deaths in the series, an operative mortality of 1.7 per cent. He was able to ascertain the present status of 210 cases, none of which had been operated upon less than 2 years previously. Of this group menorrhagia recurred in 10 cases, 5 of which subsequently required hysterectomy. In 8 cases new fibroids developed after the operation, but in 2 of these no further surgery was required. His experience makes him believe that the tendency to the formation of fibroids is a passing phase in the uterine tissues and not a continuous defect, otherwise myomectomy would be bound to fail in a very large proportion of the cases, whereas he has found recurrence quite rare. He believes that in most instances the nuclei of all the fibroids a woman is ever going to grow are laid down by the time she has reached 30 years or a little over. It follows that when myomectomy is performed on patients in the twenties or early thirties the fibroid-forming tendency has not yet gone into abeyance and the chance of the formation of new tumors is on this account considerably greater than when the operation is performed on patients over 34 years of age, especially when the number of tumors removed at the first operation has been considerable. On the other hand, it is in just these young patients that the desirability of saving the uterus is greatest, and if surgery can restore their marriage value for even a few years or enable them to have even one child, a great gain is effected, even if hysterectomy is necessary later. Of 77 patients in whom conception was desired 30, or 39 per cent, did conceive after myomectomy. In regard to the technique which he uses, it is interesting to note that a clamp is applied to the lower uterine body which compresses both uterine arteries at the same time. By this means, together with the application of ring forceps on each ovarian artery, all four main vessels are temporarily controlled, so that the field of operation will be practically bloodless and the operator can work deliberately without loss of blood and with the field of operation unobscured by hemorrhage. The uterine clamp is applied from the pubic end of the abdominal incision, and it is essential that the round ligaments should be included in its grip, otherwise the tightening causes it to slip down on the conical cervix until finally it is compressing the vagina below the uterine arteries. The clamp and forceps are not removed until the suturing of the uterus is completed. When they are taken off there is a certain amount of oozing from the suture holes, which soon ceases after the uterus is returned to its place. Whenever possible, the primary incision should be single and median through the anterior wall of the uterus in order to prevent adhesions to other intraperitoneal organs. Tumors not directly accessible through the median anterior incision are reached by secondary incisions made from the primary incision. In the majority of cases he believes that it is advisable to open and explore the uterine cavity in order not to miss a small submucous myoma or polypus, and thus, perhaps, leave behind the chief cause of the menorrhagia for which the operation is being performed. The opening of the uterine cavity will not increase the risk of the operation unless the uterus is already infected, in which

event myomectomy should never be attempted. Tumors of the posterior wall are often removed through this incision into the uterine cavity. Following the removal of large myomata, the remaining portion of the uterus must be reconstructed by trimming away superfluous tissue and by careful obliteration of the remaining cavities. For the latter purpose Bonney prefers tier sutures of catgut. His paper is concluded with a description of his various methods of dealing with unusual types of fibroids, which should be carefully read by those contemplating this type of surgery.

OTO-RHINO-LARYNGOLOGY

UNDER THE CHARGE OF
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Observations on Semon's Law. Derived from Evidences of Comparative Anatomy and Physiology.—In masterful style, NEGUS (*J. Laryngol. and Otol.*, 1931, **46**, 1) presents a scholarly, detailed and comprehensive contribution designed to unravel the history of the laryngeal muscles, to describe their functions, and to distinguish between the primitive and the more recently acquired duties. Stating that "the evidence of comparative anatomy is strongly in favor of its truth," the author takes as the basis of his discussion Semon's law. This law depends "on the proclivity of the abductor fibers of the recurrent laryngeal nerve to become affected sooner than the adductor fibers, or even exclusively, in cases of undoubted central or peripheral injury or disease to the roots or trunks of the pneumogastric, spinal accessory, or recurrent nerves." This observation demonstrates that if the recurrent laryngeal nerves, which supply the intrinsic are partially deranged in their function, the individual may be able to carry on movements of closure but not movements of dilatation on one or both sides of the larynx according to whether one or both nerves are affected. The outstanding factors in support of Semon's law are the observations that the sphincteric muscle band of the larynx serves a vital function, on which depends the very existence of the individual, and it is of more ancient origin than its antagonists—the dilators. Although admitting the limitations of his subject in the field of practical utility, Negus points out certain very important clinical adaptations—such as the possibility of death from asphyxia in bilateral paralysis of the abductor muscles; the value of estimating the alveolar CO_2 or the alkali reserve of the blood as an index for surgical intervention; the prevention of posttracheotomic respiratory failure by the administration of CO_2.

Relation of Infection of the Ear and Infection of Intestinal Tract in Infants.—"Infection of the mastoid antrum is *not* the cause of acute intestinal intoxication in infants." Such is the conclusion of WISHART (*J. Am. Med. Assn.*, 1930, **95**, 1084), the physician-in-chief and his

research department, and the pathologist and his department at the Hospital for Sick Children, Toronto. After an intensive, comprehensive and impartial study over a 5-year period, the medical staff of the above-mentioned hospital believes that the type of acute intestinal intoxication in infants is the same as that which exists in other parts of Canada and in the United States. It was found that a "cold" rarely attended the onset of the disease; that most of the infants showed no clinical manifestations of upper respiratory tract infection during the span of their toxicity; that there was no correlationship between the bacteriologic findings of the upper respiratory and intestinal tracts; that many infants were free of otitic infection during the entire course of the illness; that the incidence of mastoiditis in these cases of acute intestinal intoxication is not high; that bilateral mastoidectomy as a cure for this condition was a failure; that a mastoidal operation is indicated only if an infant has typical signs of mastoiditis; that operation is not necessarily urgent, even in the presence of an acute streptococcic infection; and that operation is to be postponed as long as possible. Incorporated in the article is such a noteworthy statement as: "Our medical staff has now seen so many sufferers from this disease *with normal middle ears and mastoid antrums* that it refuses to allow the *mastoids of infants* with acute intestinal intoxication to be operated on unless they exhibit true clinical mastoiditis. Furthermore, it is stated that "Evidence is being accumulated to show that the disease (acute intestinal intoxication—Ed.) is of intestinal origin."

RADIOLOGY

UNDER THE CHARGE OF
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Electrosurgical Destruction of Recurrent Lymphoid Tissue After Tonsillectomy.—HOLLENDER (*Arch. Phys. Ther., Roentgen Ray, Radium*, 1930, **11**, 600) points out that incomplete tonsillectomies are constantly being performed. Pieces of tonsillar tissue are found in the fossæ. The patients are usually victims of certain systemic infections, such as rheumatism, cardiac disease and nephritis. Repeated exacerbations of sore throat and tonsillitis are also common. Secondary removal by the dissection method is successful and finally leaves clean fossæ in a certain number of cases. In an equal number a further recurrence is observed. In this latter class surgery cannot again be entertained, and the author regards surgical diathermy as the ideal procedure. Electrodesiccation or electrocoagulation may be employed. If a large amount of tissue is to be destroyed electrocoagulation is preferable. For small masses of lymphoid tissue, electrodesiccation is the method

of choice. Gradual disappearance of the lymphoid mass can be observed at successive examinations. Too much tissue should not be destroyed at a single treatment, as the method calls for gradual destruction without severe reactions or discomfort.

The Value of the Roentgen Ray Examination in Pulmonary Tuberculosis.—Next to the demonstration of tubercle bacilli in the sputum, characteristic Roentgen ray findings are the most positive evidence of pulmonary tuberculosis, according to RIGLER (*Minnesota Medicine*, 1930, **13**, 25). A negative Roentgen ray examination is the best evidence against pulmonary tuberculosis that can be obtained. When symptoms of tuberculosis are present the Roentgen ray examination is almost always positive. Every patient with symptoms suggestive of pulmonary tuberculosis should have an adequate Roentgen ray examination, regardless of a negative physical examination. The Roentgen ray findings frequently do not indicate whether the tuberculous lesion is active; this may better be determined by the clinical signs. The roentgen examination gives an accurate picture of the extent and type of tuberculosis present. It is an invaluable aid in determining the type of therapy to be used, the effects of therapy and the course of the disease. Fluoroscopy is of little value in the diagnosis of early cases, and stereoscopic films are imperative.

Intravenous Urography and Uroselectan.—Six cases in which intravenous urography was employed are described by LEWIS, CARROLL and SCHATTYN (*Radiologic Review*, 1930, **52**, 337). The authors consider the method well adapted to patients so weak that they cannot bear instrumental ureteropyelography, and to those in which cystoscopy is impracticable for any reason. It is improbable that cystoscopic urography will ever be supplanted entirely by the intravenous. The writers have already met with cases in which they would have been misled completely if they had relied on uroselectan; on the other hand, the intravenous method has revealed important conditions that probably would have been overlooked by the retrograde method. It is therefore obvious that each has its sphere of usefulness and advantage. Observation of a considerable number of films indicates that the cystoscopic negatives are usually much clearer and more distinct than those made by the intravenous method. Their evidence is on the positive side while much of the intravenous evidence is on the negative side, which is by no means as direct and forceful as the positive.

Deep Roentgen Ray Therapy of Mammary Carcinoma—Five-year Results.—From their study of 175 cases EVANS and LEUCEUTIA (*Am. J. Roent. and Rad., Therap.*, 1930, **24**, 673) conclude that Roentgen therapy is of considerable aid as an auxillary to surgical procedures in the treatment of operable mammary carcinoma. In the cases without glandular involvement the addition of irradiation does not seem to increase noticeably the five-year results above those of surgery alone, assuming that all diseased tissue is removed. But in the carcinomas that have spread to the axillary or high thoracic lymph nodes, the five-year results are almost doubled. The best method of procedure is a combina-

tion of radical surgery with a thorough systematic irradiation of the entire anterior thorax, axilla and neck on the diseased side. In the inoperable or recurrent carcinomas, Roentgen therapy produces prolongation of life if the lesion is localized to the adjacent lymph nodes or anterior thorax, and alleviates the symptoms if the carcinoma is already generalized.

The Effect of Roentgen Rays on the Thyroid and Parathyroid Glands.—From their experimental studies WALTERS, ANSON and IVY (*Radiol.*, 1931, **16**, 52) conclude that the histology of the normal thyroid of the dog is not materially altered by a Roentgen ray dosage known to be of value in certain cases of hyperthyroidism. The tendency of the effect was in the direction of hyperplasia. The treatment caused a definite hyperplasia of the parathyroids. A gradual slight decrease in blood calcium occurred in spite of the parathyroid hyperplasia. It is pointed out that these results do not necessarily apply to the hyperplastic thyroid of Graves' disease.

Deep Roentgen Ray Treatment of Chronic Gonorrheal Infection in the Female.—Six cases of gonorrheal infection of the vagina, urethra and cervix were subjected to deep Roentgen ray therapy by HENRY (*Radiol.*, 1931, **16**, 47). The results in all cases were practically the same. The erosions disappeared from the cervix, the discharge became very thin, and the general health improved. Smears taken over a period of four months after treatment failed to reveal the presence of gonococci in 5 of the 6 patients. One patient menstruated three weeks after treatment; 2 after six months; 1 after seven months; and 2 after one year. One patient became pregnant three months after treatment. The infections in the 6 cases had existed for two to nine years.

Roentgenologic Appearance of Interlobar and Mediastinal Encapsulated Effusion in the Thorax.—FREEDMAN (*Radiol.*, 1931, **16**, 41) states that interlobar effusions are characterized roentgenologically by sharply defined band or wedge-shaped or circular shadows in the region of the interlobar septa. They require to be distinguished from lobar and marginal pneumonia, caseous consolidations and bronchial carcinomas. Mediastinal pleural effusions are represented by band-, wedge-shaped or triangular shadows parallel to the vertebral column or to the cardiac silhouette. They are imitated more or less by pericardial effusions, paravertebral abscesses, aortic aneurysms mediastinal tumors and areas of bronchiectatic consolidation.

Blood Changes in the Leukemias and the Lymphomata and Their Bearing on Roentgen Therapy.—Roentgen irradiation, according to ISAACS (*Am. J. Roent. and Rad. Therap.*, 1930, **24**, 648) stimulates primitive myeloblasts and lymphoblasts to rapid reproduction. Myelocytes and small lymphocytes are stimulated to finish their life history and they then die or are excreted. The matured cells are excreted into the gastrointestinal tract—polymorphonuclear cells into the mouth, lymphocytes into the intestines. Very rapid excretion may result in a decrease of the number of cells in the peripheral circulation (leukopenia) giving the false impression of an aplastic bone marrow.

NEUROLOGY AND PSYCHIATRY

UNDER THE CHARGE OF

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A Brief Résumé of the Types of Insanity Commonly Met With in India, With a Full Description of "Indian Hemp Insanity" Peculiar to the Country.—EDULJI DHUNJIBHOY and BOMB (*J. Ment. Sci.*, 1930, **76**, 254) lists the types of insanity in the order of their frequency as met with in a mental hospital in India. The order as given is: Manic-depressive psychosis; dementia præcox; toxic psychoses (*a*) hemp, (*b*) alcohol, (*c*) secondary to starvation and physical exhaustion, (*d*) infection, pregnancy and the puerperium; mental defectives; epilepsy; paraphrenia and paranoia; primary and secondary dementia; senile, traumatic and arteriopathic psychoses; encephalitis lethargica; general paralysis; psychoneuroses. The author comments upon the rarity of general paresis and states that he has never seen a case in an Indian who had never been abroad, but has seen 2 cases in those who had traveled. The description of "Indian Hemp Insanity" follows. He describes two types—acute mania and chronic mania, together with a secondary dementia. The primary symptomatology in acute mania is an intense excitement accompanied by visual and auditory hallucinations usually referring to beautiful women who talk and copulate with the patient. The attack is of shorter duration and relapses are infrequent if the drug is stopped at once and recovery is the rule. Complete amnesia for all events is found on recovery. There is a characteristic dare-devil demeanor with an irresistible impulse to wilful damage. There is a history of the drug habit, and absence of a psychopathic or neuropathic history. In addition, a peculiar eye condition is seen in which there is a conjunctival congestion of the horizontal vessels of both eyes. In the chronic mania the symptoms are less severe but there is a general expansivity. Complete loss of speech, lasting for a prolonged period after recovery, is sometimes seen, and one case is cited in which speech was lost for eight years. In the more chronic forms the acute congestion of the eye vessels is replaced by a well-marked line of blood pigments in the same situation. The prognosis is very hopeful. In the acute cases 90 per cent recover while in the chronic cases about 40 per cent recover. Postmortem examination revealed no gross abnormalities. Treatment is complete removal of the drug as no withdrawal symptoms are manifested.

Hypophrenia as a Symptom of Juvenile Paresis.—POTTER (*The Psychiat. Quarterly*, 1931, **5**, 1) presents 11 cases of juvenile paresis wherein he demonstrates the importance of syphilis as one of the etiologic factors in psychiatric problems in children—especially among the mentally defective class. He states that there is a generally pre-

valent opinion among physicians in charge of institutions for care and treatment of the mental defective that syphilis has little, if any, causal relation in mental deficiency. The reason for this opinion, he explains, is that there has been too much dependence placed upon statistics and not enough attention given to detailed clinical examination and interpretation of facts. The cases in his series are presented briefly from a clinical point of view and leave no doubt concerning their diagnosis. Each exhibits the presence of parental syphilis, the presence of the characteristics of retardation, a low intelligence quotient, positive physical findings and significant serological studies. From this material he draws the conclusions that: (*a*) direct infection of the central nervous system (neurosyphilis) in cases of congenital syphilis occurs with such sufficient frequency that it is not to be regarded as a rare or uncommon phenomena; (*b*) congenital cerebral syphilis always results in mental pathology; (*c*) the mental pathology of cerebral syphilis may be expressed by various gradations of hypophrenia usually accompanied by emotional instability without any outstanding psychotic manifestations; (*d*) the organic neurologic symptoms of congenital neurosyphilis may be expressed by either a well-defined hemiplegia on the one hand or merely exaggerated patellar reflexes and sluggish pupils on the other; (*e*) the serologic findings in the blood and spinal fluid depend on the relative activity of the syphilitic process—that in some cases both the blood and spinal fluid Wassermann is strongly positive with lymphocytosis, albumin and a paretic or luetic type of gold chlorid curve in the spinal fluid, while the other extreme may be found in other cases in which the only positive serology is manifested by a weakly positive paretic or luetic gold chlorid curve in the spinal fluid; (*f*) a history of parental syphilis is always present and the characteristic history of miscarriages, still births and other evidence of congenital syphilis is commonly obtained with reference to the siblings of the patient; (*g*) when the central nervous system is invaded by the syphilitic infection in early childhood, infancy or even *in utero*, the mental symptomatology is confined almost exclusively to the field of intelligence even when the involvement is of a parenchymatous type.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Pituitary Factor in Arteriosclerosis. Its Experimental Production in Rabbits.—Several workers had previously produced arteriosclerosis in rabbits, by feeding diets high in fat or lipoid substances. It had also been noticed that a marked hyperplasia of the suprarenal

cortex with a lipoid storage took place in arteriosclerosis, hypertension and nephritis. Thus the importance of suprarenal cortex and cholesterol metabolism was suggested. MOEHLING and OSIUS (*Ann. Int. Med.*, 1930, **4**, 578) knowing the close relationship between the pituitary gland and fat and carbohydrate metabolism, suggested that the pituitary secretion was a factor in arteriosclerosis. The authors desired to show the correlation between the pituitary and suprarenal glands in the production of arteriosclerosis. A series of four groups of healthy rabbits were used. The first group was used as a control, and fed on a normal laboratory diet. The second group was fed on a high cholesterol diet. The third group was fed on the same high cholesterol diet plus the addition of a daily injection of 1 cc. of pituitrin (posterior lobe extract). The fourth group was fed on a normal laboratory diet plus the addition of daily injection of 1 cc. of pituitrin. The animals were kept on such a routine for one hundred days and then autopsied. The authors were able to demonstrate that with the injection of posterior lobe extract alone, even without the influence of diet that a marked suprarenal cortex hypertrophy took place which they believe is an important link in the production of arteriosclerosis. The authors also showed that marked atheromatous plaques could be produced in the rabbit's aorta, within a period of one hundred days by feeding a diet high in cholesterol along with a daily injection of posterior lobe pituitary extract.

Etiology of Disseminated Sclerosis.—Ever since Charcot described disseminated sclerosis as a distinct morbid entity, numerous attempts have been made to discover a specific etiologic agent. Spirochetes were at one time considered as possibly responsible but the evidence failed to support this view. Focal infections in tonsils (Woodbury, 1919) and about the teeth (Dor. 1924) have been thought to be responsible but this factor has not been accepted as of prime importance. A specific neurotropic virus has been advanced by many as possibly the type of agent active in this disease. The recent report of CHEVASSUT (*Lancet*, 1930, i, 552) aroused considerable interest because of her claim that she had not only discovered the specific virus but had succeeded in obtaining cultures of it. She described the morphologic and biologic characteristics of the "virus" and vaccines were prepared which PURVES-STEWART (*Lancet*, 1930, i, 560) used as a specific treatment in his patients with disseminated sclerosis. In temporary conjunction with HICKS and HOCKING (*Lancet*, 1930, i, 612) certain studies were made of pathologic and biochemical changes produced by this "virus" which did not lead to any definite or very helpful conclusions. (The Abstractor had the opportunity to visit the laboratories of Westminster Hospital where this work had been carried out and after investigating the subject for about four weeks and consulting with many of the leading medical research workers in London his conclusions were: there is no proof that the causative agent has been discovered; the controls used were inadequate; many attempts to confirm Chevassut's results have failed and the evidence of a curative value of the vaccines is quite incomplete. The characteristic tendency of disseminated sclerosis to undergo spontaneous remissions, sometimes of very long duration,

makes it particularly difficult to evaluate any method of treatment. In this particular method involving as it does the intravenous or intrathecal administration of a "specific vaccine" which from the nature of the materials used cannot exclude the element of shock, will demand the most rigid statistical study because on the clinical results obtained rests the burden of proof that a virus has been discovered. This is true even if the various phases of the study of "cultures" could be repeated by others, or clean-cut evidence were available that the phenomena described are to be obtained exclusively with the cerebrospinal fluid from patients with disseminated sclerosis.) At a meeting of the Royal Society of Medicine CARMICHAEL (*Brit. Med. J.*, 1931, i, 97) opened a discussion on the above subject, which at least indicated that much more must be done before the work of Chevassut and her associates can be accepted as reliable evidence that the agent of disseminated sclerosis has been discovered.

Studies of Skin Reactions in Hypersensitiveness.—In attempting to differentiate between the types of anaphylactic and tuberculin reactions DIENES (*Proc. Soc. Exper. Biol. and Med.*, 1930, **28**, 72) has studied the histologic changes especially during the first hours after the injection of antigen and found marked differences. The anaphylactic type of reaction with a quickly developing and transient wheal is followed, after the development of edema and the vascular changes, by a more or less intense accumulation of leukocytes which is sometimes well-developed one to two hours after the injection. An accumulation of mononuclear cells (more intense in tuberculous animals) comes after the macroscopic reaction has subsided. The tuberculin reaction is different. If it is slight there occurs a strong accumulation of mononuclear cells around the bloodvessels, often before any macroscopic sign of the reaction. After twenty-four hours, even in very slight reactions, the whole reacting area is markedly infiltrated with mononuclear cells and more or less polymorphonuclear leukocytes in the center, depending upon whether the reaction is strong or weak, but always associated with the mononuclear cell infiltration. Even in reactions with central necrosis the early stages are as described and the leukocytic reaction follows tissue injury. Tuberculous guinea-pigs sometimes give this type of reaction even after normal saline. It is in the order and degree of these cellular reactions that the differences in the two types of reactions are to be found. In a second report (Same, p. 75) the author studied the sequence of events in tuberculous guinea-pigs in which egg white was introduced into the tuberculous lesions. He found the immunization process was more rapid and often there developed a strong tuberculin type of skin sensitiveness to egg white never seen in normal animals. This stage is followed by the other manifestations of sensitiveness, viz.: acute anaphylaxis, anaphylactic type of skin reaction, the protracted anaphylactic shock and the appearance of antibodies in the serum. These results suggested that in normal animals a phase corresponding to the tuberculin sensitiveness might occur and may have been overlooked. In support of this he found five to seven days after treatment that the slight skin reactions were suggestive of very slight tuberculin reactions in that they often are delayed

and persist for forty-eight hours. Carefully timed preparations of these reacting areas gave the evidence of a mononuclear cell response at the site of injection and a relatively slight influence on the circulation. The author concludes that the tuberculin type of skin sensitiveness is probably an exaggerated development of this first phase of the immunization process and is therefore of great interest in the study of immunity in infectious diseases.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Psittacosis: Epidemiologic Considerations With Reference to the 1929–1930 Outbreak in the United States.—ARMSTRONG (*Public Health Reports*, 1930, **45**, 2013) notes briefly the earlier occurrence of psittacosis in the United States and gives the outstanding features of the 1929–1930 epidemic in considerable detail. There were recorded 74 foci of infection with a total of 169 cases, with 33 fatalities; these were distributed among 15 states and the District of Columbia, but they do not include laboratory infections. It is insisted that psittacosis is a clinical entity, and one not readily confused with ordinary pneumonia, and that birds are etiologically related to its occurrence in man. Parrots occasioned by far the larger number of cases, with parrakeets, "love birds," and canaries contributing a few cases each. It is stated that many thousands of birds are imported annually and that they come from many tropical and subtropical countries. The infectiousness of the disease from birds to man is very high but from man to man almost *nil*. The incubation period is ordinarily ten days, but varies from six to fifteen days. The disease is more prevalent among women than among men, doubtless due to better opportunities for contact. The clinical symptoms are described as follows:

The disease may begin suddenly with chilly sensations, fever and headache, or these may appear after a few days during which the patient has not felt exactly well. The fever when first recorded is usually 100° to 102° F. and tends with irregular remissions to rise to a height of 103° to 105° during the second week. The pulse is likely to be slow, considering the temperature. Nosebleed is not uncommon. Focal lung lesions with physical signs may be present at the first examination or appear after three or four days. There is usually but little cough or expectoration early, but these may develop later.

The cough is usually nonproductive. Chest pains may be present. The tongue, as a rule, presents a heavy white to brownish coat, with red edges, but may be cracked and dry. The appetite is lost and constipation is the rule. Abdominal distention is troublesome in many cases. Albuminuria is a very constant accompaniment after the disease is established, and retention may be present. "Rose spots" have been occasionally reported.

The blood count is usually normal or slightly above normal during the first few days, but a leukopenia is the rule later on. In one case the count was as low as 600 cells on the twentieth day of illness, but counts from 3000 to 5000 are more common. Delirium is common when the temperature is high; stupor may be present. Dreams are likely to disturb the sleep, and insomnia may be troublesome. The fever may terminate after about eight days or continue for three weeks or more. The following table shows the relative frequency of occurrence of the more common symptoms as reported for the 169 cases:

MOST FREQUENTLY RECORDED SYMPTOMS IN 169 CASES.

Symptom.	Number of cases in which present.	Number of cases in which absent.	Unknown.
Headache	112	13	44
Malaise	107	14	48
Cough	106	23	40
Chills	98	25	46
Pains other than head	95	28	46
Anorexia	92	24	53
Constipation	87	36	46
Coated tongue	85	20	64
Delirium or stupor	48	69	52
Nosebleed	25	96	48
Diarrhea	13	110	46

Relapses. Relapses are not uncommon. Three of the 11 Hygienic Laboratory cases suffered relapses during the first three weeks following the return of the temperature to normal. The relapses began with symptoms similar to the original onset but ran milder courses, the temperature rising to 100° to 102° F. and then gradually falling in a few days. A relapse occurred in another case in Washington after three weeks of normal temperature. These four relapses occurred among some 13 cases treated with convalescent serum, and one wonders if this form of treatment predisposes to relapse.

Complications. Phlebitis is the most common complication. The death rate is about 24 per cent in persons over thirty, but no death occurred below that age.

Antirabic Vaccine Paralysis.—McCOY (*Pub. Health Rep.*, 1930, **45**, 1888) gives the following as the chief theories as to the cause of this condition: (*a*) That it is due to anaphylaxis resulting from the injection of foreign animal tissue (rabbit's cord); (*b*) that it is due to a "toxin" elaborated by the specific organism of rabies; (*c*) that it is due to rabies resulting from street virus received at the time the bite was inflicted; (*d*) that it is due to rabies resulting from fixed-

virus infection; (*e*) that it is due to infection with extraneous organisms introduced with the virus during treatment; (*f*) that it is due to hysteria and other neuropsychologic disorders. Perhaps at the present time one would like to add the suggestion that the antirabic vaccines may activate a virus lying dormant in the body or may serve to enhance susceptibility to an ordinarily nonpathogenic virus. Another thought that will occur to one familiar with the frequency of pathologic processes in the central nervous system of rabbits is the possibility of the occasional susceptibility of man for a virus normally, or perhaps we had better say, commonly, found in rabbits. There were 8 cases of paralysis among about 25,000 treatments, but no evidence to incriminate any special form of treatment.

A Study of Ventilation and Respiratory Illness in Syracuse Schools: With an Analysis of Factors Affecting Criteria Used.—The New York State Commission on Ventilation, in its 1923 report, presented data which suggested that the system of fan ventilation commonly installed in American schools is not only unnecessary but undesirable. The work of the Commission appeared to indicate that respiratory disease among pupils is actually more prevalent in fan-ventilated schools than in schools provided with a simpler and more economic system of window supply and gravity exhaust. So far as the main issue is concerned, observations of a similar trend have been made by three independent observers: Greenburg, at New Haven, Conn., Childs, at Cleveland, Ohio, and Shaughnessy, at Chicago. Recently the Commission has devoted itself to the study of certain other types of ventilation and of certain modifications of fan ventilation (*Am. J. Hyg.*, 1930, **12**, 196). Conditions have been observed in three furnace-gravity schools, one fan-gravity school and two fan-fan schools for 3 years, and in one other fan-gravity school, two other fan-fan schools and two window-fan schools for 2 years and in two other fan-gravity schools for 1 year. In this study of Syracuse schools a group of oldfashioned schools ventilated by furnace inlets and gravity exhaust ducts shows in each of 3 years lower absence rates due to respiratory disease than did groups of more modern schools ventilated by either plenum or exhaust fans. On analysis, it appears that the observed differences were due in part to the fact that the furnace-gravity schools were situated in districts largely inhabited by a foreign-born population. If, however, allowance be made for this factor, these schools still show an apparently lower respiratory disease absence rate than that of the mechanically ventilated schools. However, the authors are not disposed to stress the better record of these schools. It is evident that the comparison of different schools is open to serious errors and one can rarely be certain that all such errors have been eliminated.

Rate of Air Flow and Room Temperature in Relation to the Health of School Children.—The results of this study by the New York Commission (*Am. J. Hyg.*, 1930, **12**, 215) are largely negative ones; but it is believed that they are of value as a contribution to the technique involved in such investigations. They appear to indicate that respiratory illness absenteeism and even data in regard to respiratory illness

in attendance may yield concordant and significant results if child populations be balanced as to age, sex and nationality stock and if observations be made by the same observer in the rooms compared. The correlation between absenteeism due to respiratory illness, absence and respiratory illness in attendance (+0.54, −0.07) and the harmony between the results obtained under equivalent conditions indicate that the measures used were essentially significant. The results differ from those of our earlier New York work and agree with the results of Greenburg and Shaughnessy in failing to show that slight differences in schoolroom temperature exert appreciable effects on the prevalence of respiratory disease. This conclusion does not, of course, negative the results of other studies, both clinical and statistical, which clearly demonstrate the harmful effects of marked overheating. There was no evidence that the cutting down of air flow in fan-ventilated schools from 30 to approximately 15 cubic feet per pupil per minute affected the health of the pupils. The results suggest on inspection that full-flow rooms are superior to reduced-flow rooms, but this conclusion proves to be unfounded, since the probable errors of the means are greater than the differences between them. We are left with the conclusion that the reduction by one-half of the standard air flow of 30 cubic feet gives no significant indication of an unfavorable effect on the health of the pupils as measured by respiratory illness.

PHYSIOLOGY

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SESSION OF MAY 18, 1931.

Age Changes in Inorganic Constituents of Sound Human Teeth.—HELEN M. LUNDSTROM (from the Laboratory of Physiology, University of Pennsylvania). Chemical analyses are reported on 42 whole human teeth, confined to mandibular and maxillary incisors, selected for freedom from imperfection and secured from healthy individuals. In these preliminary studies no attempt was made to remove enamel from dentin. The composition of teeth differs from that found previously in bone. The data when arranged with reference to increasing age, indicate that the inorganic composition changes more with respect to Mg and CO_3 than to Ca and PO_4. With reference to the percentage composition of dry, fat-free, unashed teeth, an increase of 50 per cent in Mg, a decrease of 20 to 25 per cent in CO_3, a slight increase in P and a fair constancy in Ca was shown. The Mg changes with reference to Ca and CO_3 with reference to PO_4. The general trend of the variations in the composition of teeth with respect to increase in age is an increase in Mg with relation to Ca and increase in PO_4 to CO_3.

Is Osmotic Hemolysis an All-or-none Phenomenon?—ARTHUR K. PARPART (from the Laboratory of Physiology, University of Pennsylvania). Studies on the kinetics of osmotic hemolysis have as one of their fundamental assumptions the concept that at the time of hemolysis the cell liberates all of its hemoglobin. The literature on the nature of hemolysis contains scanty and conflicting data. This lack of agreement, combined with the fact that some of the best of the present methods for study of the rate of hemolysis depend on the opacity changes accompanying the disappearance of the cell, has necessitated a more definite knowledge of the relation between the disappearance of the cell and the amount of hemoglobin liberated.

By a careful control of the various sources of error, and by the use of dilute solutions which permit a practically complete outward diffusion of hemoglobin at the time of hemolysis, it has been possible to show that osmotic hemolysis produced by hypotonic NaCl solutions is accompanied by a complete liberation of hemoglobin from the cell, both during the course of hemolysis and at equilibrium.

Osmotic hemolysis, when induced by a penetrating substance of small molecular volume, *e. g.*, ethylene glycol, is also of an "all-or-none" character. Penetrating substances of large molecular volume, *e. g.*, glycerol, cause an "all-or-none" type of hemolysis when the system is at equilibrium. Before the attainment of equilibrium, however, there is a slight tendency for a retention of hemoglobin which is possibly due to a blocking of the outward diffusion of a portion of the hemoglobin by the large molecules of the penetrating substance.

No evidence has been secured of a "partial" liberation of hemoglobin during hemolysis. Other workers who have pictured a hemolysis of this type have used concentrated suspensions of cells, and under such circumstances, when hemolysis occurs, the hemoglobin merely diffuses to equilibrium with the surrounding fluid and hence there must of necessity be a considerable retention within the cells.

Spontaneous Insulin Resistance in Rabbits: The Effect of Thyroidectomy on the Response to Insulin.—ISOLDE T. ZECKWER (from the Department of Pathology, University of Pennsylvania). The experiments reported are a continuation of the studies reported at the meetings of the American Association of Pathologists and Bacteriologists, April 2 and 3, 1931.

Two rabbits were encountered that showed spontaneous resistance to insulin. One required 20 units for the development of convulsions, the other required 76 units. With subconvulsive doses the blood sugar remained for many hours near the convulsive level, but apparently release of glycogen from the liver, which is generally conceded to be due to activity of the sympathetic nervous system in which the adrenals are concerned, was more active in these rabbits than in normal ones, and in consequence sufficient glycogenolysis occurred to avert convulsions.

Twenty-nine days after thyroidectomy 2 units of insulin were sufficient to cause convulsions in the rabbit that previously had required 20 units; 17 days after thyroidectomy 5 units were sufficient in the rabbit that had previously required 76 units. Thyroidectomy, therefore, increased the response to insulin roughly 10 and 15 times, while,

according to Burn and Marks, normal rabbits show an increase in response to insulin after thyroidectomy of 6 and possibly 9 times, and so far as our experiments have progressed Burn and Marks' figures have not been exceeded in the normal rabbit. The thyroid, therefore, seems to be one factor in this phenomenon of spontaneous insulin resistance, and these results tend to support the view that the thyroid influences the sensitiveness of the response of the sympathetic nervous system.

However, these resistant rabbits after thyroidectomy still did not respond to the very small doses of insulin to which a normal rabbit responds after thyroidectomy, so that there must be other factors than the thyroid concerned in this insulin resistance.

Carotid Sinus Reflexes and Respiration.—Carl F. Schmidt (from the Laboratory of Pharmacology, University of Pennsylvania). Perfusion of the carotid sinuses of 15 dogs with Ringer's fluid, or with blood taken from and returned to a donor dog, has regularly shown respiratory depression or apnea on raising sinus pressure, stimulation sometimes very marked, on lowering it, the effect intensified by section of the vagodepressor nerves, entirely abolished by denervation of the sinuses. Similar results were obtained in 2 cats, but in a rabbit there were no respiratory effects, though circulation was very markedly influenced. This confirms Heymans' observations (*J. Physiol.*, 1930, **79**, 254; *Arch. internat. de pharm. et de therap.*, 1930, **39**, 400), that reflexes from the carotid sinuses can affect respiration profoundly. Heymans' conclusion, that respiratory responses to changes in blood pressure are wholly due to carotid sinus and aortic reflexes, has been shown to be too sweeping by four sorts of experiments: (1) Adrenalin causes apnea in dogs, cats and rabbits whose vagodepressor or depressor nerves are cut and whose carotid sinuses are completely denervated, and acetyl cholin and nitroglycerin cause marked respiratory stimulation in the same animals; in perfusion experiments (dogs) adrenalin injected intravenously is more depressant to respiration when carotid sinus pressure is low than when it is high. (2) Apnea is produced in the dog and cat when occluded vertebral and carotid arteries are released, and the effect is exactly the same whether the occlusion is made proximal to the carotid sinuses (common carotids) or distal to them (external and internal carotids), or whether the sinus nerves are intact or cut; CO_2 inhalation reduces somewhat the apnea consequent upon release of the vessels after carotid sinus denervation, but the apnea is by no means prevented thereby, showing that it is not due to loss of CO_2 during the occlusion. (3) Abrupt increase in intracranial (cisterna magna) pressure in the dog to a level equal to or exceeding arterial blood pressure causes hyperpnea and apnea occurs when intracranial pressure is abruptly lowered; smaller rises in intracranial pressure, to half arterial pressure or even less, cause definite respiratory stimulation. (4) When the brain of the rabbit is perfused by way of the internal carotids with the animal's own blood, by means of a pump, respiration is markedly stimulated by reduction and markedly depressed by increase in pump output, though the carotid sinus nerves are excised and the depressor nerves are cut. There may be other reflexes from

cerebral vessels or meninges, but these effects are certainly not dependent wholly upon aortic depressor or carotid sinus reflexes (Heymans); apnea is produced by release of occluded carotid and vertebral arteries in decerebrated dogs and cats after sinus denervation, so that the reflexes, if they exist, must arise in the brain stem. Change in blood supply of the center seems the more probable explanation.

Heymans (*Arch. int. de pharm. et de therap.*, 1930, **39**, 400) found the respiratory effects of changes in blood-gas tension to depend largely upon carotid sinus reflexes in dogs. In 5 crossed-circulation experiments on dogs no evidence of such dependence could be obtained, though sensitivity to pressure changes was established in all. Heymans' positive results could be duplicated in dogs only if blood from the donor was allowed to enter the cerebral circulation of the recipient (3 experiments) and occlusion of the vascular communication abolished the "reflex" effect. In two similar experiments on cats, however, there were marked reflex effects like those described by Heymans in dogs.

It seems necessary to conclude that in the respiratory effects of changes in blood pressure both reflex and central blood flow influences are concerned, and the problem becomes one of quantitative evaluation of the two. Carotid sinus reflexes to respiration are aroused (in crossed-circulation experiments) by changes in pressure amounting to about 10 per cent; when the pressure change is maintained respiration gradually escapes from the reflex influence, and the response depends upon change in pressure rather than upon any given pressure level. Attempts at evaluating the blood flow factor have been made upon 7 dogs, measuring cerebral venous outflow from the torcular herophili; the results so far have been obscured by unaccountable spontaneous changes in cerebral venous pressure and outflow. Evidence now at hand suggests that the aortic depressor and carotid sinus nerves may be extrinsic afferents to a cerebral vasomotor nervous mechanism, and that their function is to antagonize the tone of bloodvessels supplying vegetative areas of the brain, the effective stimulus being pressure in aorta and carotid sinus. This possibility is under investigation.

Observations on Living Lymphatic Capillaries in the Rabbit.—E. R. and E. L. Clark (illustrated in part by motion pictures taken by E. A. Swenson and E. R. Clark) (from the Department of Anatomy, University of Pennsylvania). In the new tissue which invades the space left in the modified type of transparent chamber introduced into the rabbit's ear (*Anat. Rec.*, 1930, vol. **47**) new lymphatic capillaries have been observed and their mode of growth, morphologic characteristics and some of their physiologic properties have been studied microscopically with daily photographic and camera lucida records over periods of weeks and months. So far as known this is the first time in which it has been possible to observe the finer microscopic details of lymphatic capillaries in the living mammal.

Studies to date have revealed the following facts:

1. Lymphatic vessels grow by endothelial sprouting. Pushing out of protoplasmic tips from preëxisting lymphatic endothelium has been observed repeatedly with the oil-immersion lens. Mitotic division of the endothelial nuclei of the tissues of lymphatic capillaries has been

observed and the times of the different phases recorded. Following the division the daughter nuclei always remained attached to the vessel wall.

2. The invasion of a new area by lymphatic capillaries is subsequent to that of fibroblasts and new bloodvessels by days or weeks. In cases in which they followed closely behind bloodvessels they were found to grow between the vessels and to form a loosely anastomosing plexus completely independent of the bloodvessel network. In cases where their invasion of the observation area was delayed the lymphatics grew in a loose space just adjacent to arteriole or venule. In either case the number of new lymphatic sprouts was much less than that of the new blood capillaries.

3. Lymphatic capillaries are normally closed at the tip. However, following injury openings have been produced in the walls of certain vessels which persisted for as long as a week; through these the passage back and forth of hundreds of erythrocytes to and from the space beyond the growing zone of vessels was observed. In every case such artificial openings eventually closed.

4. Movement of lymph in the newly formed lymphatic vessels is very sluggish—frequently the same leukocytes or erythrocytes remained in a capillary for several days. Erythrocytes and polymorphonuclear leukocytes showed degenerative changes inside the lumen of the lymphatic capillaries within two to five days.

5. In inflammatory conditions the lymphatics were observed to show dilatation accompanied by stasis.

The back-and-forth movements of blood cells inside the lymphatic capillaries, together with circulatory changes in neighboring bloodvessels were shown in motion pictures.

In addition, motion pictures were shown of active contractions of arteriovenous anastomoses present in two of the transparent chambers in which the early formation of bloodvessels and their subsequent changes had been followed over a period of 10 months.

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